Acta Scientific Women's Health (ISSN: 2582-3205)

Volume 3 Issue 6 June 2021

Case Report

The Linkage between Metachronous Thyroid and Breast Cancers: An Illustrative Case

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Received: May 11, 2021

Published: May 26, 2021

Abstract

Breast cancer (BC) is the most common cancer in women. Thyroid cancer (TC) is relatively rare with female predominance. These two malignancies often occur metachronously. This association is no more a simple coincidence. However, the reasons behind this association are not well elucidated.

We report a case of metachronous breast and thyroid cancer occurring in a postmenopausal woman. It was an invasive ductal carcinoma for the breast and anaplastic cancer for the thyroid.

We tried to find out what might be the linkage between these two malignancies.

Keywords: Thyroid; Breast; Metachronous Cancers

Introduction

Both BC and TC are common malignancies among women. These cancers often occur metachronously. A bidirectional relationship has been elucidated since the sixties [1]. It has been reported that females with a history of TC exhibit more risk of developing a second primary BC compared to females with no history of cancer [2]. Some other studies showed an increased risk of TC in BC women [3,4]. Although the reasons behind this association are not yet well understood, a combination of genetic, hormonal, environmental and therapeutic factors seems to be implicated. We tried to investigate what might be the linkage between these two malignancies through an illustrative case of a 56-year old woman who developed a lethal anaplastic TC nine years after a first invasive ductal BC.

Case Report

In December 2007, a post-menopausal 56 years old female sought medical consultation with left breast lump as the main complaint evolving for 2 months. In medical history, we noted a hypertension. The woman was obese with BMI= 32. Examination found a 2 cm lump of the upper outer quadrant of the left breast associated with a 1 cm firm axillary lymph node. Mammography examination was suspicious. Fine needle aspiration of the breast lump concluded an invasive ductal carcinoma. Thoracic-abdominal-pelvic CT and bone scan ruled out any metastasis. The patient received 6 cycles of CMF (cyclophosphamide-methotrexate-5FU) followed by radical mastectomy with axillary lymph node dissection. Post-operative outcomes were simple. The histopathological exam confirmed the diagnosis of invasive ductal carcinoma. The margins were free and the lymph nodes were metastatic. The ER, HER and PR status were negative. An adjuvant RT was performed. In July 2016, the patient presented with a rapidly enlarging swelling of the neck associated with dyspnea and dysphagia. Cervical CT showed a voluminous process of the left thyroid infiltrating the trachea and the larynx and a 2 cm nodule of the right lobe (Figure 1). Biopsy of the cervical mass concluded an anaplastic carcinoma. A palliative treatment based on chemoradiation therapy, tracheostomy and feeding gastrostomy was undertaken. The patient died 3 months later after cataclysmic cervical bleeding.

Discussion

Primary multiple cancer associating BC and TC are in a constant increase [5,6]. The relationship between the two malignancies is bidirectional. Garner identified among 1604 TC patients 60 with

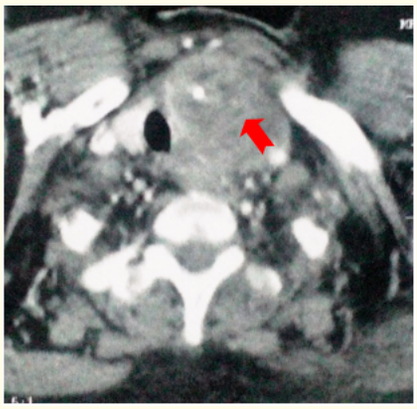

Figure 1: CT scan axial section: a locally advanced left thyroid tumor infiltrating the trachea, the larynx and the adjacent muscles.

co-existing BC [5]. In the same perspective, Zhang., *et al*. found among 18732 BC patients, 217 cases of double metachronous primary cancers [7]. TC was the most frequent malignancies associated with BC according to these authors. Kim., *et al*. reported that female with a history of TC exhibits more risk of developing a BC [2]. In a recent study, it has been reported that women with BC are two-folds more likely to develop a TC [8]. Inversely, women with TC have 67% more chances to develop a BC [8].

Metachronous cancers are secondary malignancies developed 6 months or more after the first primary cancer. In our case, the time lap between the 2 malignancies was 9 years. Raymond., *et al*. reported mean interval between the 2 malignancies equals to 6.2 years [9].

BC and TC are common female cancers with postmenopausal peak. In metachronous cases of BC and TC, the first cancer tends to be diagnosed at a young age [10]. It was not the case for this woman as she developed the first cancer at 56 years.

Genetics seem to have a great role in genesis of BC and TC. It has been reported in a Swedish study that first-degree relatives of females diagnosed with BC are at an increased risk of developing TC [11].

Mainly reported genetic defects shared by TC and BC were:

- H23 gene overexpressed in BC malignant tissue as well as in papillary TC tissue [12].
- TRα and TRβ receptor genes of thyroid hormones [13].
- RET/PTC1 over expressed in papillary TC tissue as well as in malignant BC tissue [14].

Thus, a genetic and family investigation is highly recommended when a member develops double primary breast and thyroid malignancies.

Both BC and TC are hormone-dependent cancers. Up regulation of estrogen and progesterone receptors was implicated in BC. These sex steroid receptors were found in human thyroid tissue with a higher level in malignant tissue than normal tissue [15]. Other studies concluded that the expression of cell cycle-related genes and proto-oncogenes in thyroid cells could be under estrogen control regulation, which could contribute to the development of TC [16].

Obesity and lack of physical activity are risk factors for BC [17]. Obesity, like in this case, was reported as a risk factor in epithelial-derived thyroid cancers [18]. Similar to TC, iodine-rich diet seems to have a protective role against BC. BC cells display the same sodium-iodide symporter found in thyroid cells [19]. Iodine-rich seaweed was described as an apoptosis inductor in human BC cells with greater potency than that of fluorouracil used in the treatment of BC [19]. This hypothesis was supported by the low rate of BC in Japan where the diet is rich in iodine seaweed.

Radiation is well known as a major risk for TC [20]. The risk of developing TC is increased in the 5 to 10 years after radiation therapy for the first cancer [21]. In this case, the patient developed TC 9 years after radiation therapy for BC. In 80% of cases, radiation-induced TC is of papillary type [21]. Progression from papillary to anaplastic cancer, like in this case, could be favored by P53 mutation. This same mutation was also seen in BC [22].

Finally, it seems that radioactive I^{131} used for the treatment of TC is not associated with the secondary development of BC [23].

Conclusion

Association between BC and TC is no longer a simple coincidence. These two malignancies are connected through common epidemiological, environmental, hormonal and genetic factors. Oncologists, head and neck surgeons and gynecologist should be aware of this association in the follow-up of survivors of TC or BC. Future prospective studies are needed to better understand the relationship between these 2 cancers.

Conflict of Interest

The authors declare no conflict of interest.

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Volume 3 Issue 6 June 2021