

Concomitant Metastatic Squamous Cell Carcinoma and Invasive Breast Carcinoma of the Axillae in a Patient with History of Breast Cancer Treated with Mastectomy and Hormone Therapy

Crista Horton* and Nicholas Tranakas

Broward Health Imperial Point, 6401 N. Federal Highway, Fort Lauderdale, FL, USA

*Corresponding author: Crista E. Horton, Broward Health Imperial Point, 6401 N. Federal Highway, Fort Lauderdale, FL, USA. E-mail: chorton@browardhealth.org

Received: June 12, 2023; **Accepted:** June 26, 2023; **Published:** July 10, 2023

Abstract

Currently there are no clear guidelines regarding the management of multiple primary malignancies when they occur simultaneously. Furthermore, there have been no cases to date describing axillary breast cancer recurrence in combination with metastatic axillary squamous cell carcinoma (SCC) of unknown primary origin. Both of these cancers are rare and associated with poor outcomes. Treatment for both SCC and breast cancer axillary metastasis includes a combination of axillary lymph node dissection, radiation, and chemotherapy. We describe here a woman with prior hormone-receptor-positive breast cancer who completed a 5-year course of aromatase inhibitor therapy and had a prior mastectomy with negative sentinel lymph nodes, who then presented with a rapidly growing axillary mass. Pathological analysis demonstrated recurrent breast cancer and metastatic SCC.

Keywords: Breast cancer; Squamous cell carcinoma; Axillary recurrence; Metastasis; Metachronous cancer; Synchronous cancer; Targeted therapy

Introduction

Breast cancer is the most commonly diagnosed cancer in women and the second most common cause of death among women in the world [1]. For patients with locoregional recurrence (LRR) of breast cancer, LRR in the breast parenchyma is associated with better outcomes than extramammary recurrence [2]. Studies indicate that rates of axillary recurrence in cases in which sentinel lymph node biopsy (SLNB) was negative and patients did not undergo a complete axillary lymph node dissection (ALND) are similar to recurrence after ALND alone [3]. Squamous cell carcinoma (SCC) with unknown or known primary origin metastasizing to the axillary lymph nodes is rare, with poorly characterized management and outcome [4]. Treatment for both breast carcinoma or SCC metastatic to the axillae is with axillary lymphadenectomy and adjuvant radiation to the area with systemic chemotherapy [5,6].

The frequency of multiple coexisting primary tumors of all types is estimated to be 2-17%, and breast cancer coexists with tumors of non-breast primary origin at 4.1% [7]. Addressing multiple primary tumors is challenging due to the need to plan a therapy strategy that does not add toxicity or potentially negative pharmacologic interactions. Herein we describe an interesting case of a woman with prior Estrogen receptor positive, Progesterone receptor positive (ER/PR+) breast cancer history, prior bilateral mastectomies, and negative axillae on SNLB, who completed a five-year course of aromatase inhibitor therapy, then six years later developed a primary recurrence of a metastatic breast carcinoma and concomitant metastatic squamous cell carcinoma in the left axillae. Notably, this case is, to our knowledge, the first documentation of concomitant recurrent invasive breast carcinoma and metastatic squamous cell carcinoma to the same location in the axillae, presenting as a rapidly growing mass.

Case Description

An 81-year-old woman presented with a new, palpable left axillary mass with no other symptoms. She noticed the mass while applying antiperspirant in the morning and denied the presence of the mass just one week prior. She had a history of left-sided breast cancer (T2N0M0, ER/PR+) treated with bilateral mastectomies with left axillary SNLB six years prior to this presentation. She completed a five-year course of anastrozole in 2021. The patient indicated weight loss of 40 pounds in the past year, with associated anorexia. She underwent ultrasound-guided core needle biopsy of the mass, which measured approximately 5.2 x 4.6cm. Pathological analysis from the biopsy identified core fragments of poorly differentiated metastatic SCC with extensive necrosis. Further, Ki67 staining indicated a high proliferation index at 30%, and the tumor suppressors P16 and P53 were robustly expressed, which raised suspicion for HPV-associated SCC or an unknown primary tumor of that of the skin, lung, or head and neck regions.

Two weeks later, the patient underwent left axillary completion lymphadenectomy, in which multiple metastatic matted lymph nodes were identified intraoperatively. Using blunt dissection and a bipolar vessel-sealing device, lymph nodes from axillary levels one, two, and three were taken, including Rotter's nodes, with necessary sacrifice of the first intercostobrachial nerve due to its involvement with the matted lymphatic tissue. Pathological analysis returned with nine out of sixteen lymph nodes positive for metastatic breast carcinoma, with a largest deposit of 1.1cm in diameter with extra-nodal extension. Additionally, one out of sixteen lymph nodes was positive for metastatic squamous cell carcinoma with marked keratinization and necrosis, with deposit of 2.2cm in diameter. The breast carcinoma demonstrated expression of the estrogen receptor (ER,100%), progesterone receptor (PR, 95%), no expression of HER2, and robust Ki67 expression (90%).

After follow up with her surgeon and oncologist one month later, she then underwent positron emission tomography with computed tomography (PET/CT) in order to evaluate her for a possible unknown primary source of the squamous cell carcinoma and to detect potential metastasis of the breast carcinoma. PET/CT demonstrated no metabolically active lymph nodes in the head or neck region. She had no metabolically active lesions in the mediastinal or internal mammary lymph nodes. However, she did have postsurgical changes to the left axillary region, with a 8.90mm FDG avid subcentimeter lymph node in the left axillae that demonstrated maximum SUV values ranging to 3.2, which could suggest a small metastatic lymph node in that location (Figure 1). Metabolically active lesions were not seen in the lungs, liver, adrenal glands, spleen, nor were any retroperitoneal, mesenteric, or pelvic lymph nodes seen, nor any in the skeleton. She then underwent local radiation therapy to her left axillae. She was started on fulvestrant, an estrogen receptor downregulator, and palbociclib, a small molecule inhibitor of the cell cycle.

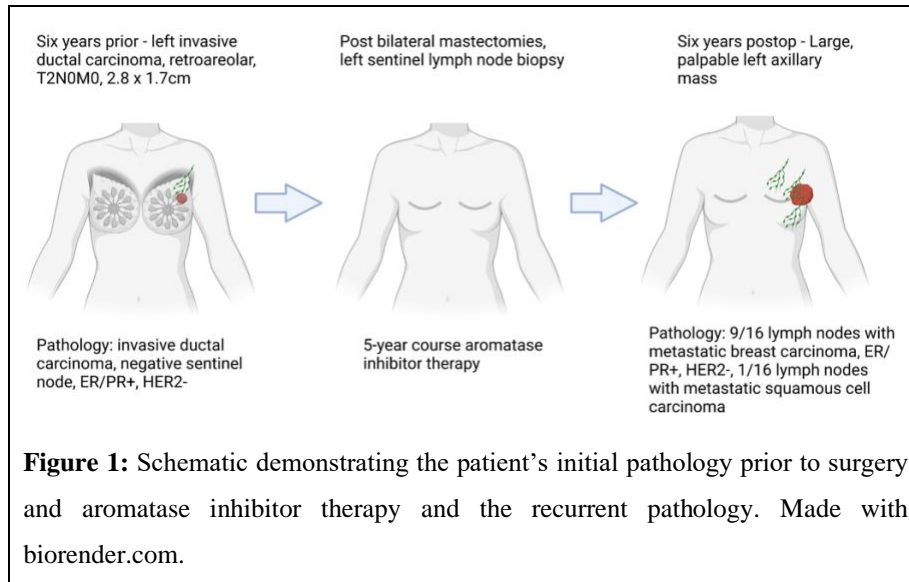


Figure 2: Postoperative PET/CT demonstrated changes in the left axillae after surgery and possible left axillary lymph node metastasis, as indicated by the yellow circle. There are no other hypermetabolic areas on the scan indicative of a primary tumor.

Discussion

Metastatic SCC existing simultaneously with invasive breast carcinoma and arising as a large, rapidly growing mass in one week's time is perplexing. Axillary recurrence of breast cancer is rare but significant following breast cancer treatment, and it is associated with a median survival time of five years [8]. Factors correlating with improved disease-free and overall survival rates include time to recurrence greater than 2.5 years, no initial axillary radiation, asymptomatic presentation of the recurrence, and treatment of isolated axillary recurrence with axillary radiation and systemic treatment [8]. Fortunately, many of these factors applied to this patient. Furthermore, the metastatic SCC and the recurrent breast cancer were located together in the axillae, which made surgical planning and targeting the axillae for radiotherapy less complicated than had different locations been involved.

The concept of multiple primary tumors is not new, and it goes back to a study in 1921 which showed that there were 4.7% multiple primary cancers found in 3,000 cases of malignancy [9]. Despite the long-standing nature of this problem, no clear treatment guidelines have been established for multiple primary cancer types. When patients have multiple active primary tumors, establishing a diagnosis and deciding treatment to treat both without adding morbidity is challenging. Unfortunately, given their complexity, patients with multiple primary tumors are excluded from clinical trials with novel therapeutics [7]. For this reason, there are limited data to guide treatment in patients with multiple primary malignancies, and approaches are not yet based on prospective clinical trial evidence [7]. Rather, a personalized approach is taken with combinations of systemic, targeted, or supportive therapies based on tumor profiling, anticipated problems, and significance of each malignancy for the patient [7]. As life expectancy increases, the incidence of patients with multiple primary malignancies is likely to increase as well [10]. Identifying germline and somatic mutations as well as commonalities among synchronous and metachronous cancers is becoming increasingly important in order to utilize personalized strategies including targeted therapies and checkpoint inhibitors [7].

Conclusion

Physicians and surgeons must understand that in patients with complex medical histories, there may be overlap of multiple disease processes, knowledge of which is essential in treatment planning.

REFERENCES

1. Siegel RL, Miller KD, Jemal A. Cancer statistics. *Ca Cancer J Clin.* 2018; 68: 07-30.
2. Wapnir IL, Anderson SJ, Mamounas EP, et al. Prognosis After Ipsilateral Breast Tumor Recurrence and Locoregional Recurrences in Five National Surgical Adjuvant Breast and Bowel Project Node-Positive Adjuvant Breast Cancer Trials. *J Clin Oncol.* 2006; 24: 2
3. Palesty JA, Foster JM, Hurd TC, et al. Axillary recurrence in women with a negative sentinel lymph node and no axillary dissection in breast cancer. *J Surg Oncol.* 2006; 93: 129-132.
4. Wach MM, van Beek E, Ayabe R, et al. Metastatic squamous cell carcinoma of known and unknown primary origin treated with axillary or inguinal lymphadenectomy. *Am J Surg.* 2018; 216: 963-968.
5. Goyal A, Duley L, Fakis A. Axillary treatment for patients with early breast cancer and lymph node metastasis: systematic review protocol. *World J Surg Oncol.* 2013; 11: 06.

6. Beydoun N, Graham PH, Browne L. Metastatic Cutaneous Squamous Cell Carcinoma to the Axilla: A Review of Patient Outcomes and Implications for Future Practice. *World J Oncol.* 2012; 3: 217-226.
7. Vogt A, Schmid S, Heinimann K, et al. Multiple primary tumours: challenges and approaches, a review. *Esmo Open.* 2017; 2: e000172.
8. Konkin DE, Tyldesley S, Kennecke H, et al. Management and Outcomes of Isolated Axillary Node Recurrence in Breast Cancer. *Arch Surg-Chicago.* 2006; 141: 867-874.
9. Owen LJ. Multiple malignant neoplasms. *JAMA.* 1921; 76: 1329-1333.
10. Liu Y, Chen Y, Yen S, et al. Multiple primary malignancies involving lung cancer—clinical characteristics and prognosis. *Lung Cancer.* 2002; 35: 189-194.