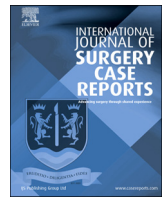




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Contralateral axillary lymph node metastasis in second primary Breast cancer: Case report and review of the literature



Jacob Gingerich*, Edna Kapenhas, Jack Morgani, Alan Heimann

Department of Durgery Radiology Pathology, Southampton Hospital, Southampton, New York, United States

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ABSTRACT

The rare entity of contra-lateral axillary lymph node metastasis (CAM) has been a debatable topic in the realm of breast cancer management for many years. There remains controversy over whether CAM should be considered distant metastasis or locoregional spread. It is also uncertain why or how CAM occurs. In this case report and review of the literature, we present an 81-year-old female with an apparent second primary breast cancer with synchronous CAM. This paper describes a scenario of altered lymphatic drainage which likely lead to CAM. In this situation, we propose that CAM should be treated with curative intent rather than stage IV disease. We also attempted to gain a better understanding of the histopathology and tumor characteristics of tumors associated with CAM. Our patient was treated with curative intent and remains disease free for over 18 months. This supports the theory that patients with distorted lymphatic drainage from prior interventions who have CAM, should be treated as locoregional extension of the disease.

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1. Introduction

Contralateral axillary lymph node metastasis (CAM) is uncommon with literature citing the incidence to be between 1.9 and 6% [1]. CAM has been broken down into synchronous CAM (found at time of primary diagnosis) and metachronous CAM (recurrence after primary treatment). There has been conflict in the literature if CAM should be considered distant disease and thus treated as a stage IV breast cancer rather than locoregional extension of contralateral breast cancer. When a cancer is found in the contralateral axilla, there are 3 main potential sources: contralateral spread from the original breast tumor, metastasis from an occult primary in the contralateral breast, and metastasis from an extramammary site.

We present a case report, using the SCARE guidelines, of an 81-year-old female in a community hospital setting with an apparent second primary breast cancer with synchronous CAM [11]. This case report with a review of the literature proposes that altered lymphatic drainage may contribute directly to CAM, and in these situations, CAM should be treated with curative intent. We also attempted to gain a better understanding of the histopathology and tumor characteristics of tumors associated with CAM.

2. Presentation of case

An 81-year-old Caucasian, female was referred to the outpatient breast clinic after a recent finding of metastatic cancer in a left axillary lymph node confirmed on biopsy.

She has a history of invasive ductal carcinoma of her right breast 18 years prior to presentation. The tumor was found on routine mammography and there were no other lesions seen on imaging at that time. She has no family history of breast cancer. She underwent a lumpectomy with sentinel lymph node biopsy, radiation therapy, as well as 5 years of Tamoxifen at that time. Final pathology revealed a 1 cm poorly differentiated invasive ductal carcinoma as well as small areas of DCIS and LCIS. The tumor was ER/PR positive, and Her-2 negative. One sentinel node and 4 additional axillary lymph nodes were negative for metastasis.

At presentation to the breast clinic, she had no palpable masses on physical exam. On routine mammography, the patient was found to have prominent left axillary tail lymph nodes which were not seen on her prior yearly surveillance mammograms. There were no suspicious lesions seen in either breast on mammography. An ultrasound guided core biopsy of the left axillary lymph nodes found metastatic lobular carcinoma with signet ring cell features (Fig. 1). The cells were ER/PR positive, Her2 negative, and Ki-67 was 20%. A PET/CT showed numerous normal-sized not hypermetabolic left axillary lymph nodes and no evidence of distant metastasis. A breast MRI revealed a 2 cm irregularity in the lateral right breast as well as multiple left axillary lymph nodes with enhancement in the region of the biopsied lymph node (Fig. 2). A second look right breast ultrasound confirmed the MRI abnormality and a subsequent

* Corresponding author.

E-mail address: jacob.e.gingerich@gmail.com (J. Gingerich).

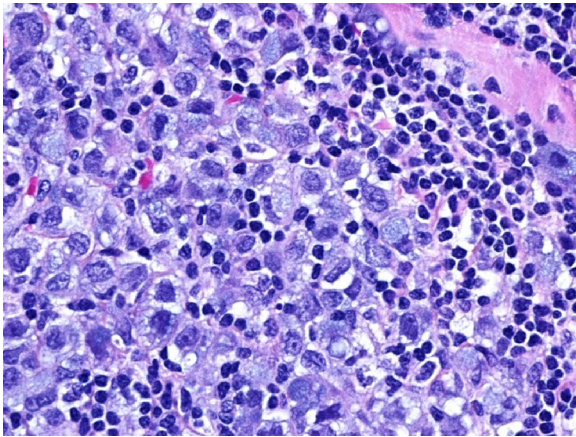


Fig. 1. High power view of left axillary lymph node biopsy.

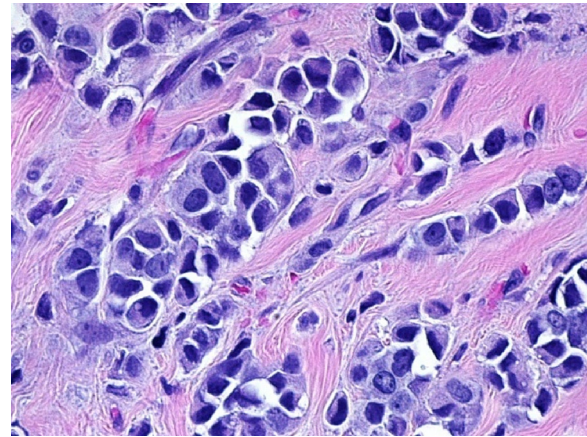


Fig. 3. High power view of right breast specimen displaying infiltrating lobular carcinoma.

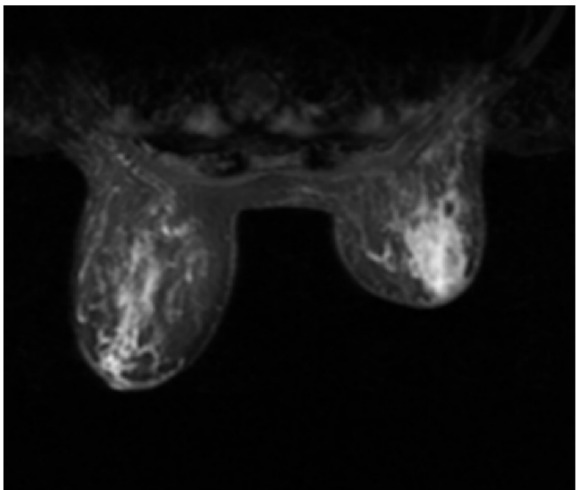
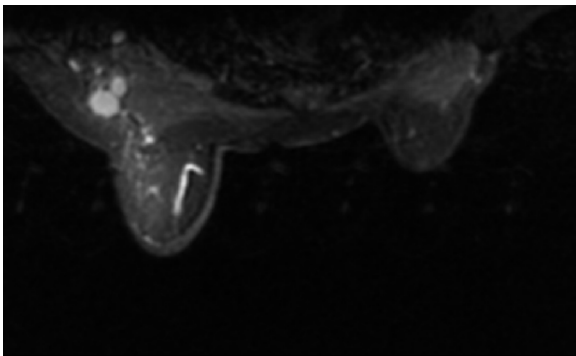


Fig 2. MRI imaging displaying prominent left axillary lymph nodes as well as right breast lesion.

ultrasound-guided biopsy revealed moderately differentiated invasive lobular carcinoma with signet ring cells, ER/PR positive, Her2 negative, and Ki-67 was 20%, consistent with the contralateral lymph node metastasis (Fig. 3). Lymphoscintigraphy with injections of 100 uCi of Tc99 M Tilmanocept (Lymphoseek) revealed no axillary lymph node uptake bilaterally.

The patient underwent a right total mastectomy and left axillary lymph node dissection. Pathology revealed a 22 mm right breast invasive lobular carcinoma. One benign lymph node was removed from the right axilla. The left axillary node dissection revealed 29/44 lymph nodes with metastatic lobular carcinoma.

The patient received 8 treatments of cyclophosphamide, methotrexate, and 5-FU and then underwent left breast, axilla, and lower cervical/supraclavicular lymph node radiation. Following the completion of chemotherapy and radiation, she was started on exemestane. Follow-up surveillance imaging includes yearly mammography as well as yearly MRI imaging. She remains disease free at 18 months post-op.

3. Discussion

Although ipsilateral axillary lymph node metastasis in breast cancer is relatively common, contralateral axillary lymph node metastasis (CAM) is quite uncommon. Literature reports the incidence to be anywhere from 1.9% to 6% [1]. Of the cases of CAM reported in the literature, the overwhelming majority are metachronous CAM, making synchronous CAM even more uncommon. The true incidence of

CAM is difficult to estimate. The rates may be overestimated due to lack of MRI for diagnosis of occult contralateral tumors. On the other hand, the incidence may be underestimated because patients may ignore physical exam findings or fail to have adequate follow-up [1].

In most literature reports, CAM is associated with aggressive histopathological features of the primary breast tumor. Both Morcos et al. and Huston's series report histopathologically aggressive tumors associated with CAM. Morcos et al. reports 81% having a tumor grade of 3, 81% having lymphovascular invasion, and larger primary breast tumors with 95% being T3 or T4 lesions [2]. They also report increased incidence of hormone receptor negative and Her-2 positive lesions compared to breast cancers without CAM [2,3]. When comparing this data to the patient presented in this case report, it is important to note that in both Morcos et al. retrospective paper and Huston's case series, nearly all patients had metachronous CAM. Zhou et al. present a case of synchronous CAM with hormone receptor positive and HER-2 negative characteristics [4]. This suggests that there is a wide variability in histopathological findings with CAM, and that perhaps synchronous vs. metachronous CAM may represent different disease processes and different primary tumor aggressiveness.

In a study of sentinel node drainage patterns in patients with breast cancer previously untreated, the lymphatic drainage of the breast was as follows: ipsilateral axillary (92.3%), internal mammary (21.1%), interpectoral (2.1%), infraclavicular (2.6%) and supraclavicular (0.4%) [5]. Alterations to these drainage routes may be apparent following radiotherapy or previous operations. The patient presented had previous axillary surgery and radiotherapy.

Tokmak et al. confirmed that following radiotherapy and surgeries involving the axilla, there is a greater propensity for nodal drainage outside of the ipsilateral axilla [6]. In 1972, Haagensen et al. hypothesized that breast cancer could disperse to the contralateral axilla by permeating the deep lymphatic plexus of the chest wall [9]. Tokmak et al. found 2 out of 330 (0.6%) patients with contralateral axillary drainage on lymphoscintigraphy. Both patients had either a previous sentinel lymph node (SLN) biopsy or axillary lymph node dissection (ALND) [6]. In Maaskant-Braat et al's meta-analysis of SLN biopsies in locally recurrent breast cancer, aberrant drainage was found in 43.2% of patients [8]. This confirms that the alterations to the lymphatic drainage may be more important in patients with CAM rather than the aggressiveness of the tumor.

Based on the information above, one could conclude that CAM due to altered lymphatic drainage and aberrant pathways is secondary to lymphatic rather than hematogenous spread. With that theory in mind, one could begin treating CAM with a curative

intent rather than a palliative intent. The AJCC cancer staging manual used to classify CAM as distant disease, however, in the most recent version there is no classification for CAM whatsoever [10]. This again suggests that if a patient develops synchronous CAM without evidence of systemic metastasis, the treatment could be considered curative.

Although there are no large studies on patient outcomes and treatment modalities due to the rarity of the disease, there are several small series that demonstrate treatment options. Wang et al. reviewed 28 cases of CAM reporting extremely poor prognosis. They report >70% relapse rate, and they found a 25% mortality rate within 2–3 years due to distant metastasis [1]. They found that radiotherapy and systemic chemotherapy or hormone therapy may be of most benefit rather than ALND or mastectomy. There was no difference found in recurrence-free survival of

patients who underwent ALND, but patients who underwent radiotherapy doubled their median recurrence-free survival from 10 to 22 months [1]. Dayyat et al. theorize that radiotherapy may be effective for 2 reasons; first it may treat any occult ipsilateral breast cancer as well as eradicate microscopic disease in the dermal lymphatics that could have spread from the contralateral primary tumor [7]. In both Wang et al's and Morcos et al. data there were significant systemic metastasis leading to death in many cases.

Based on the metastasis rate Wang et al. proposes that systemic treatment with chemotherapy and hormone therapy, when appropriate, should be an integral part of management of CAM.

4. Conclusion

CAM is a rare disease entity, and it presents a challenge in the therapeutic decision making process. In the case presented, the patient was treated as though the contralateral axillary nodes were a regional spread of the cancer rather than distant metastasis. With the history of previous axillary surgery and radiation, our patient supports the theory that CAM often occurs due to distortion of the normal lymphatic drainage of the breast. As such, the patient was treated with a curative intent. The early success of this treatment supports the theory that CAM in the presence of altered lymphatic drainage is indeed a regional spread of the disease. Although large studies are difficult to assess the treatment of CAM due to its rarity, we propose that in cases where the lymphatic drainage has been altered by previous surgery or radiation therapy, patients should be treated with curative intent.

Conflict of interest

There is no conflict of interest with any of the authors involved in this paper.

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Ethical approval

No ethics approval was needed.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

Jacob Gingerich and Edna Kapenhas contributed by writing the paper.

Jack Morgani contributed by providing radiologic images.

Alan Heimann contributed by providing pathologic images.

Guarantor

Edna Kapenhas.

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