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Sentinel node mapping and biopsy in ectopic axillary breast cancer: A case report and review of the literature

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Abstract

Sentinel lymph node mapping in patients with axillary breast carcinoma is technically challenging and poorly described in the literature. We report a patient with primary ectopic breast carcinoma of the axilla in whom concurrent peri-tumoral and intra-tumoral injection of radionuclide tracer allowed for identification and biopsy of sentinel lymph nodes.

Introduction

Ectopic accessory breast tissue can occur anywhere along the embryonic mammary line and is found in 2-6% of the general population.(1) Though rare, cancer can arise in ectopic breast tissue, with 70-80% of these cases arising in the axillary region.(2) Once detected, ectopic breast cancer is managed under the same principles as orthotopic breast cancer. One approach involves the option of wide local excision with sentinel lymph node (SLN) biopsy followed by radiation therapy. However, SLN mapping and biopsy in axillary breast cancer can be challenging due to the proximity of the primary tumor to the axillary lymph nodes. Few studies have described the injection technique of radionuclide tracer dye in the setting of axillary breast cancer. Here, we describe a case of primary axillary breast carcinoma in which concurrent peri-tumoral and intra-tumoral injection of radionuclide tracer allowed for successful identification of SLNs. This report serves to detail the approach to SLN identification in this clinical situation and adds to the growing body of evidence documenting the feasibility of SLN mapping and biopsy in ectopic breast carcinoma.

Case Presentation

A 72-year-old Caucasian postmenopausal woman was evaluated for a palpable right axillary mass that she had identified on self-examination approximately two weeks prior to presentation. The mass was non-tender and not associated with nipple discharge or any systemic symptomatology. The patient was G2P2, with menarche at age 10 and menopause at age 50. She reported a family history significant for a diagnosis of breast cancer in her sister at age 41 and niece at age 53. There was no family history of ovarian cancer. Of note, the patient's sister had negative BRCA testing. Physical examination revealed a slightly mobile mass in the right axilla located about 6 cm below the axillary crease and 1.5 cm anterior to the mid-axillary line. The patient had a thin body habitus, and the right axillary mass was located essentially in the subcutaneous layer of the skin. There was no adenopathy in the right axilla or in the bilateral cervical or supraclavicular regions. A bilateral diagnostic mammogram showed a spiculated mass measuring 0.9 cm in diameter in the extreme axillary tail of the right breast that corresponded with the palpable mass found on physical examination (Figure 1). An ultrasound of the right axilla demonstrated a hypoechoic, irregular mass with spiculated margins measuring 0.9 x 0.7 x 1.3 cm that was surrounded by marked vascularity (Figure 2). No abnormal lymph nodes were identified on mammogram or ultrasound. These findings were assigned a BI-RADS 4 classification.

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An ultrasound-guided core needle biopsy revealed a grade 2 invasive lobular carcinoma (ILC) that was ER-positive (95%), PR-negative (0%), and HER2/neu-positive by fluorescence in situ hybridization. A bilateral breast MRI was performed to rule out the presence of any other breast abnormalities. Representative T1 fat saturated post-contrast sagittal and coronal breast MRI images demonstrated an irregular enhancing mass in the right axilla (Figure 3) consistent with biopsy-proven ILC but was otherwise negative. Ultimately, the patient was determined to have a stage IA (cT1cN0) breast cancer.

After consultation with the breast medical oncology team, the patient underwent wide local excision of the right axillary mass with SLN biopsy. One hour prior to surgery, the patient was injected with 400 mCi of technetium-99m (Tc-99m) sulfur colloid. One-third of the dose was injected intra-dermally into the skin overlying the mass, one-third was injected directly into the mass, and the remaining third was injected into the subcutaneous tissue underneath/posterior to the mass. At the time of operation, the right axilla was examined and the position of the mass was noted 6 cm inferior to the axillary crease. The axilla was scanned, and an area of increased counts was identified just superior to the tumor in the mid-axillary line. An elliptical incision was created over the mass and deepened with cautery. The tumor was resected along with an ellipse of overlying skin and a rim of normal adipose tissue measuring approximately 1 cm. Additional shave margins were taken. The posterior border of the tumor consisted of the pectoralis major muscle, the fascia of this muscle having been included in the primary specimen. The axilla was scanned, and an area of increased counts was identified just under the pectoralis minor muscle against the chest wall. The clavipectoral fascia was incised and a 1 cm lymph node was identified and removed. *Ex vivo* this lymph node had counts over 900. It was sent for frozen section and ultimately came back positive for metastatic lobular carcinoma. The entire axilla was re-scanned and no other areas of tracer uptake were identified. No suspicious lymph nodes were found by palpation or inspection. The decision was made to forego axillary dissection given existing evidence showing that subsequent radiation therapy alone would be sufficient for control of the axilla.(3) Pathologic evaluation of the lymph node revealed macrometastatic carcinoma measuring 7 mm in diameter without extranodal extension. Regarding the primary tumor, pathologic evaluation revealed a grade 2, ER-positive, PR-negative, and HER2/neu-positive ILC measuring 1.6 cm in maximum diameter. Final margins were negative.

The patient tolerated the procedure well with no post-operative complications. She is now disease-free 6 months following surgery. She received six cycles of adjuvant chemotherapy consisting of a regimen of docetaxel, carboplatin, trastuzumab and pertuzumab. This treatment was followed by whole breast radiation therapy and maintenance pertuzumab/trastuzumab.

Results and Discussion

Primary ectopic breast carcinoma is rare, accounting for 0.3 to 0.6% of all breast cancers.(4) It can arise anywhere along the bilateral embryological mammary streaks where accessory breast tissue persists, the most common location being the axilla (60-70%).(5) Due to its rarity and the paucity of published data, the management of ectopic axillary breast cancer is often conducted using the same principles as orthotopic breast cancer, in which the patient may be offered a mastectomy or standard breast conservation therapy approach consisting of wide local excision and SLN biopsy followed by radiation therapy. In 2005, the ACOSG Z0011 trial demonstrated that axillary lymph node dissection may be avoided in early-stage breast cancer patients with <3 positive SLNs.(3) To identify SLNs intraoperatively, radionuclide tracers such as Tc-99m and/or blue dye (e.g., methylene blue or isosulfan blue) are injected immediately prior to surgery. These principles have been routinely applied to the patient with an axillary primary tumor, even in the absence of definitive data supporting this approach.

A major challenge with the conduct of SLN biopsy in axillary breast cancer is the choice of site for tracer injection. Even in orthotopic breast cancer, the options of peritumoral, subareolar and periareolar injections are debated. In a prospective randomized clinical trial of four hundred breast cancer patients undergoing SLN mapping and biopsy, Povoski *et al.* demonstrated that intradermal injection of 99m-Tc into the skin overlying the breast cancer resulted in a significantly greater frequency of localization and decreased time to first localization by lymphoscintigraphy as compared to the intraparynchemal or subareolar injection.(6)

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However, few reports have described the use of lymphatic mapping with SLN biopsy for ectopic axillary breast cancer, and the injection technique is rarely described. In a review of the literature, just 16 reports of SLN biopsy for axillary breast cancer were identified within 14 manuscripts (Table1).(4, 7-19) Of these 16 patients, three (19%) underwent radionuclide tracing with lymphoscintigraphy only, three (19%) underwent tracing with blue dye only, six (37%) underwent dual tracing with radionuclide and dye, and the mapping technique in four (25%) patients were unreported. Injection site was reported in just six patients.

The use of radionuclide tracer or blue dye to identify SLNs in axillary breast cancer poses a potential challenge. The proximity of the axillary tumor to the regional lymph nodes may lead to a "shine-through" effect, by which it becomes difficult to identify an area of tracer localization in the axilla as a result of the lower gamma counts from the node(s) being obscured by the higher counts at the injection site. In a report by Uenaka *et al* ., Tc-99m and indigo carmine were injected into the ipsilateral areola pre-operatively. However, the axillary SLNs were unable to be identified by lymphoscintigraphy or hand-held gamma probe during surgery due to the shine-through effect, and no blue dye-filled tracts or nodes were seen.(15) In contrast, Patel*et al.* reported that SLN biopsy was successful in three patients when periareolar injection of Tc-99m was combined with peritumoral isosulfan blue injection.(8) In a patient who had previously undergone excisional biopsy of an ectopic axillary breast cancer, Alavifard*et al.* reported that pre-operative injections of Tc-99m into both ends of a surgical scar resulted in SLN uptake as measured via gamma probe.(10) Peritumoral injection of indigo carmine was reported by Lee *et al.,* although it was not specified whether the dye was successfully taken up by the SLNs.(19)

In the present report, the tracer dose was divided into three equal portions and injected at three peritumoral sites. One portion was injected intradermally into the skin directly overlying the cancer and a second portion was injected into the primary tumor itself. A third portion was injected into the peri-tumoral subcutaneous tissues just posterior to the primary cancer. In this manner, it was theorized that multiple pathways were provided by which the tracer could enter the regional lymphatics and reach the SLNs. This approach permitted the successful identification of the SLNs intraoperatively with minimal shine-through and without the use of isosulfan blue dye. Of note, careful positioning of the gamma probe away from the injection site and toward the axillary region led to low levels of shine-through.

Conclusions

These results suggest that local injection of Tc-99m is feasible to perform SLN mapping in the setting of an axillary primary breast cancer. This report may serve as an example for future cases of ectopic axillary breast cancer in which SLN biopsy is indicated. However, further experience with this method is necessary.

Authorship

MKH, MZG, AM, CT and WEC made substantial contributions to conception and design of the report and were involved in drafting and revising the manuscript. All authors approved the final manuscript. All authors participated sufficiently in the work to take public responsibility for appropriate portions of the content. All authors agreed to be accountable for all aspects of the work.

References

1. Gutermuth J, Audring H, Voit C, Haas N. Primary carcinoma of ectopic axillary breast tissue. J Eur Acad Dermatol Venereol. 2006;20(2):217-21.

2. Francone E, Nathan MJ, Murelli F, Bruno MS, Traverso E, Friedman D. Ectopic breast cancer: case report and review of the literature. Aesthetic Plast Surg. 2013;37(4):746-9.

3. Giuliano AE, Ballman KV, McCall L, Beitsch PD, Brennan MB, Kelemen PR, et al. Effect of Axillary Dissection vs No Axillary Dissection on 10-Year Overall Survival Among Women With Invasive Breast Cancer and Sentinel Node Metastasis: The ACOSOG Z0011 (Alliance) Randomized Clinical Trial. JAMA. 2017;318(10):918-26.

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4. Jalali U, Dhebri A, Karip E, Hunt R. Ectopic breast carcinoma presenting as sebaceous cyst left axilla. BMJ Case Rep. 2019;12(1).

5. da Silva BB, dos Santos AR, Pires CG, Rosal MA, dos Santos LG, Lopes-Costa PV. Ectopic breast cancer in the anterior chest wall: a case report and literature review. Eur J Gynaecol Oncol. 2008;29(6):653-5.

6. Povoski SP, Olsen JO, Young DC, Clarke J, Burak WE, Walker MJ, et al. Prospective randomized clinical trial comparing intradermal, intraparenchymal, and subareolar injection routes for sentinel lymph node mapping and biopsy in breast cancer. Ann Surg Oncol. 2006;13(11):1412-21.

7. Nardello SM, Kulkarni N, Aggon A, Boraas M, Sigurdson ER, Bleicher RJ. Invasive mucinous carcinoma arising in ectopic axillary breast tissue: a case report and literature review. Am J Case Rep. 2015;16:153-9.

8. Patel BK, Jafarian N, Abbott AM, Khazai L, Lee MC. Imaging Findings and Management of Primary Breast Cancer in Accessory Axillary Breast Tissue. Clin Breast Cancer. 2015;15(4):e223-9.

9. Shuster M, Tse JY, Smith GP. Breast carcinoma arising in ectopic breast tissue presenting as an enlarging axillary nodule. Indian J Dermatol Venereol Leprol. 2015;81(4):422-4.

10. Alavifard R, Kadkhodayan S, Homaee Shandiz F, Dabbagh VR, Sadeghi R. Is sentinel node mapping possible in surgically removed ectopic axillary breast cancer? A case report. Nucl Med Rev Cent East Eur. 2016;19(B):29-30.

11. Munrós J, Vázquez M, Santiago P, Romay G, Acea B. Management of breast carcinoma in ectopic axillary breast tissue. Cir Esp. 2017;95(4):232-3.

12. Kuritzky A, Walheim L, Khakpour N. Cancer identified in accessory breast tissue within the mid axilla. Breast J. 2018;24(3):414-5.

13. Khan RN, Parvaiz MA, Khan AI, Loya A. Invasive carcinoma in accessory axillary breast tissue: A case report. Int J Surg Case Rep. 2019;59:152-5.

14. Piacentini F, Combi F, D'Onofrio R, Omarini C, Moscetti L, Drago A, et al. Axillary ectopic carcinoma of the breast. Report of two cases with different clinical presentation and review of the literature. OSP J Case Rep.1.

15. Uenaka N, Yamada K, Sato E, Kaise H, Ishikawa T. A case of accessory breast cancer mimicking metastatic lymph node from occult breast cancer. Edorium J Surg. 2019;6.

16. Rodrigues I, Pereira N, Varelas A, Coimbra N, Leal C, Lencastre L, et al. Ectopic breast tissue carcinoma-a case report. European Journal of Medical Case Reports. 2020;4(5):161-5.

17. Tsuji W. Metachronous bilateral ectopic breast carcinoma in the axilla: A case report and literature review. Breast Dis. 2020;39(3-4):149-53.

18. Addae JK, Genuit T, Colletta J, Schilling K. Case of second primary breast cancer in ectopic breast tissue and review of the literature. BMJ Case Rep. 2021;14(4).

19. Lee J, Jung JH, Kim WW, Hwang SO, Kang JG, Baek J, et al. Ductal carcinoma arising from ectopic breast tissue following microcalcification observed on screening mammography: a case report and review of the literature. J Breast Cancer. 2014;17(4):393-6.

Table 1. Reported cases of sentinel lymph node biopsy technique in primary breast carcinoma of the axilla.

Reference	Tracer Used	Injection Location	No. of SLNs identified b
Lee, 2014(19)	Blue dye	Peri-tumoral	7
Nardello, 2015(7)	Blue dye	NR	3
Patel, 2015(8)	Tc-99m and blue dye	Peri-areolar Tc-99m and peri-tumoral blue dye	2

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Reference	Tracer Used	Injection Location	No. of SLNs identified b
			NR
			1
Shuster, 2015(9)	NR	NR	NR
Alavifard, 2016(10)	Tc-99m	Edges of surgical scar	1
Munrós, 2017(11)	Tc-99m and blue dye	NR	1
Kuritzky, 2018(12)	Tc-99m	NR	4
Jalali, 2019(4)	Tc-99m and blue dye	NR	5
Khan, 2019(13)	Tc-99m	NR	3
Piacentini, 2019(14)	NR	NR	1
Uenaka, 2019(15)	Tc-99m and blue dye	Peri-areolar	0
Rodrigues, 2020(16)	NR	NR	2
Tsuji, 2020(17)	NR	NR	NR
Addae, 2021(18)	Blue dye	NR	NR

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