

Received: 2012.11.21
Accepted: 2013.01.10
Published: 2013.08.21

Lymphatic mapping could not be impaired in the presence of breast carcinoma and coexisting small lymphocytic lymphoma

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABDEF **Sebastian Arana**
ABCDEFG **Jorge Vasquez-Del-Aguila**
AB **Martin Espinosa**
BF **Vicente Peg**
ABDE **Isabel T. Rubio**

Breast Surgical Unit, Breast Cancer Center, Hospital Universitario Vall d'Hebron, Barcelona, Spain

Corresponding Author: Jorge Vasquez Del-Aguila, e-mail: jwvasque@vhebron.net

Patient: Female, 66
Final Diagnosis: Infiltrating ductal carcinoma • small lymphocytic lymphoma
Symptoms: —
Medication: —
Clinical Procedure: Sentinel Lymph Node Biopsy • lumpectomy • axillary lymph node dissection
Specialty: Breast cancer surgery

Objective: Rare presentation of two concomitant malignancies
Background: Lymphatic mapping of axillary breast cancer metastases in the presence of concomitant lymphoproliferative disease is still a controversial topic. Previous reports have postulated that tumor collision in the lymph nodes could lead to false-negative results of sentinel lymph node biopsy, leading to erroneous staging.
Case Report: We present the case of a 66-year-old woman with infiltrating ductal breast carcinoma and small lymphocytic lymphoma in whom we performed a lumpectomy and sentinel lymph node biopsy with Technetium-99 and 1% methylene blue, followed by axillary lymph node dissection regardless of the intraoperative status, which was negative. Final pathology confirmed the absence of lymph node metastases.
Conclusions: Previously published cases reported correct assessment of SLNB in patients with concomitant small lymphocytic lymphoma and breast carcinoma. We postulate a possible pathological explanation for this: lymphoid cell clusters with pseudofollicles or proliferative centers of small lymphocytic lymphoma are localized outside the nodal sinuses of the lymph node, maintaining its capability of draining, and thus, the feasibility of SLNB in these patients, as in the presented case.

Key words: breast cancer • lymphoid malignancies • Sentinel Lymph Node Biopsy (SLNB)

Full-text PDF: <http://www.amjcaserep.com/download/index/idArt/884000>



1225



1



1



11

Background

Lymphatic mapping with sentinel lymph node biopsy (SLNB) is a crucial step in the management of early stage breast carcinoma. It was designed to minimize the adverse effects of lymph-node surgery, but still offers outcomes equivalent to axillary lymph-node dissection (ALND) in terms of staging patients [1].

Whether SLNB is safe in patients with axillary lymph-node diseases such as lymphoma and synchronous breast carcinoma is still controversial. Previously published literature has postulated that tumor collision in the lymph nodes, which occurs when 2 different neoplasms involve the same organ, could lead to increased false-negative results of the SLN and to erroneous staging.

Tumor collision could occur in different settings: when 2 different carcinomas metastasize to the same lymph node, when tumor-to-tumor metastases occur, or when a carcinoma metastasizes to a lymph node that contains a lymphoproliferative disease [2].

In this article, we review the literature and report the case of a breast cancer patient with a concurrent low grade lymphoma that presented as a clinically palpable ipsilateral axillary lymph node.

Case Report

A 66-year-old woman with a history of low grade lymphoma diagnosed 7 months before with no treatment was referred from screening for further assessment of a 1.5cm spiculated mass, BIRADS 5, in the upper outer quadrant (UOQ) of the right breast (Figure 1).

Physical examination revealed a 2cm breast mass in the UOQ along with several bilateral adenopathies. Ultrasonography demonstrated a 1.7 cm lesion and enlarged pathological right axillary lymph nodes. CT scan and bone gammagraphy were performed, showing no metastatic disease. The patient was classified as cT1NxM0 stage. Ultrasound-guided biopsies of breast and axillary right adenopathy were performed. Pathology of the breast was reported as infiltrating ductal carcinoma grade I, positive estrogen receptor (100%) and positive progesterone receptor (100%), HER 2 negative, and Ki67 of 5%. FNA of both right axillary lymph nodes revealed a CD23, CD20 positive lymphocytic lymphoma.

The case was presented at the Breast Cancer Multidisciplinary Committee of our hospital along with the Hematology service to assess treatment options. We decided to perform SLNB with lumpectomy, followed by ALND, regardless of SLN diagnosis.

Retro-areolar injection of 4.0 mCi of Technetium-99-labeled radioactive tracer was made the day before surgery and pre-operative lymphoscintigraphy was performed. One milliliter of 1% methylene blue was injected in the retroareolar region 10 minutes before the lumpectomy. Two nodes were identified using a hand-held gamma detection probe: 1 "hot and blue" and 1 just "hot". No intraoperative study was performed.

At definitive histology, the 2 sentinel nodes were free of metastatic carcinoma, but both contained small lymphocytic lymphoma infiltrates (SLL).

The same SLL infiltrates were demonstrated in the ALND lymph nodes, where the absence of breast cancer metastasis was confirmed.

The breast specimen pathology demonstrated a 1.8cm invasive ductal carcinoma with cribriform intraductal component <25% with histological grade 1 ER+ PR+ HER-2 negative and final stage: pT1N0M0.

The patient was sent to the Lymphoma Clinic for treatment assessment. Hormone therapy and radiation to the breast was planned as part of the cancer treatment.

Discussion

The occurrence of second primary neoplasms in patients with history of malignant tumors has been well documented [2]; however, the synchronous presentation of 2 malignancies is an extremely rare event that involves approximately 0.8% of these patients [3].

In the case of breast cancer, the synchronous malignancies reported include CLL/SLL, acute myeloid leukemia, pheochromocytoma, and malignant melanoma [4]. Possible explanations of this phenomenon are the immunological impairment caused by the lymphoma, a possible common genetic or viral cause, or the stimulation by an unknown mechanism.

There are a few published references about SLNB results in the presence of a lymphoproliferative disease in breast cancer patients (Table 1).

Cheung et al. presented a case of a 55-year-old patient with an infiltrating ductal carcinoma [5]. Lumpectomy with SLNB was performed, identifying 3 SLN. Intraoperative frozen section showed no metastasis or atypical lymphoid infiltrate. Definitive pathology demonstrated a 1mm micrometastasis in 1 of the lymph nodes. ALND was performed and pathology demonstrated no further metastasis, but SLL in all the lymph nodes were the same kind of lymphoma found in our patient.

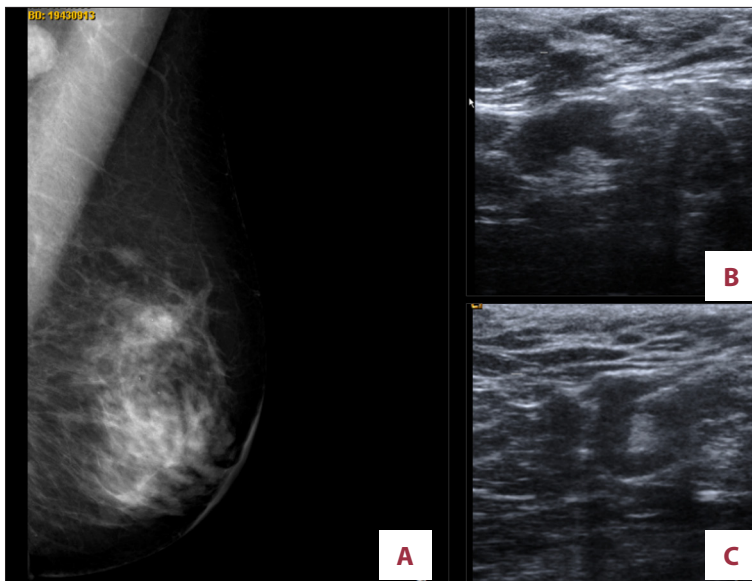


Figure 1. Radiologic findings. (A) Mammogram: Irregular defined mass in upper exterior quadrant of right breast, with visible axillary lymphadenopathy. (B, C) Axillary ultrasound showing hypoechoic, irregular lymph nodes.

Table 1. Previously reported cases and series of synchronic breast cancer and lymphoproliferative disease.

Author/year	N	Technique*	SLN N **	SNLNB analysis	Axilar lymphadenectomy analysis	Follow up
Cheung et al. 2007	1	Combined	3 blue**	1 micrometastasis and atypical lymphoid infiltrate	0/25, Chronic lymphocytic leukemia and small lymphocytic lymphoma (CD5, CD23)	1 year
Benoit et al. 2003	1	Combined	1 hot & blue 1 blue	Lymphoplasmocytic cell	1/9, Lymphoplasmocytic cell	NR
Barranger et al. 2005	1	Combined	2 hot & blue	1 metastasis	0/25, B-cell follicular lymphoma	No
Quilon et al. 2006	1	---	1	MALT lymphoma	Not performed	6 months
Sadanand Anavekar et al. 2008	1	Combined	2 hot & blue	B-Cell lymphoma	Not performed	2 years
Dy et al. 2010	9	7 combined 2 biopsy of palpable nodes	–	4 cases of SLNB accurately identified for carcinoma metastasis. No false negatives in the other cases.	7 CLL/SLL 2 Follicular	37 (24–66)

* Radioactive traser and blue dye; ** blue – stained with blue dye, hot – positive for radioactivity.

Barranger et al. demonstrated the feasibility of SLNB in this kind of patient in a 66-year-old woman with a grade 2 invasive ductal carcinoma coexisting with a follicular B-cell lymphoma in the axilla. SLNB was positive for metastatic breast carcinoma. ALND was performed and no evidence of further metastasis was found; however, all 21 nodes harvested were positive for B-cell follicular lymphoma [6].

Another 2 case reports, from Quilon et al. and Namrata Sadanat Anavekar et al., showed no metastatic disease on SLNB, and no ALND was performed in the patients [7,8].

In contrast, Benoit et al. presumed an increased risk of false-negatives due to lymphoproliferative cells infiltration in the nodal basins of the axilla. They presented the case of a patient with Waldenström macroglobulinemia and breast carcinoma who underwent SLNB. Two nodes were identified and pathology reported both as free of metastatic disease. ALND was performed and final pathology showed that 1 of the 9 non-sentinel nodes was invaded with metastatic breast cancer cells [9].

Regarding that, it has been postulated that if it is assumed that the lymphoproliferative condition occurred first (as in the

case of Benoit et al.) the obliteration of lymphatic channels by a neoplastic lymphoid population could have a role. In addition, neoplastic lymphoid cells could locally reduce tissue necrosis factor or interleukin 1 (IL)-induced adhesion of breast cancer cells to the endothelial layer of axillary lymph nodes [10].

The situation, however, is more complex because carcinomas do metastasize in lymphomatous nodes, perhaps overcoming the resistance offered by pre-existing lymphoma cells through complex interactions [10].

Dy et al. reported 9 women who underwent axillary SLN surgery for breast cancer and had a diagnosis of lymphoproliferative disease. Both positive and negative SLNs were accurately identified. They postulated that the false-negative case presented by Benoit et al. could have been the result of the known 7.3–8.4% percent false-negative rate associated with SLN surgery [4].

It also has been suggested that lymphatic channels of the node could remain at least partially patent to allow carcinoma metastasis. In this setting, we believe that the understanding of lymph-node architecture is vital to establish how B cell lymphomas may affect the lymphatic drain, and therefore the SLN.

References:

1. Krag DN, Anderson SJ, Julian TB et al: Sentinel-lymph-node resection compared with conventional axillary-lymph-node dissection in clinically node-negative patients with breast cancer: overall survival findings from the NSABP B-32 randomised phase 3 trial. *Lancet Oncol*, 2010; 11(10): 927–33
2. Wahner-Roedler d, Reynolds C, Boughey J: Collision Tumors With Synchronous Presentation of Breast Carcinoma and Lymphoproliferative Disorders in the Axillary Nodes of Patients With Newly Diagnosed Breast Cancer: A Case Series. *Clin Breast Cancer*, 2011; 11(1): 61–66
3. Dettrick A, Chern B: Synchronous Breast Cancer and Lymphoma: a case series and review of the literature. *J Clin Pathol*, 2010; 63: 555–57
4. Dy BM, Reynold CA, Wahner-Rohdler DL, Boughey JC: Sentinel lymph node surgery for staging of breast carcinoma in patients with lymphoproliferative disease. *Am Surg*, 2010; 76(12): 1423–25
5. Rodriguez Fernandez J, Martella S, Trifiro G et al: Sentinel node biopsy in patients with previous breast aesthetic surgery. *Ann Surg Oncol*, 2009; 16(4): 989–92
6. Barranger E, Marpeau O, Uzan S, Antoine M: Axillary sentinel node involvement by breast cancer coexisting with B-cell follicular lymphoma in non-sentinel nodes. *Breast J*, 2005; 11(3): 227–28
7. Quilon JM, Gaskin TA, Ludwig AS, Alley C: Collision tumor: invasive ductal carcinoma in association with mucosa-associated lymphoid tissue (MALT) lymphoma in the same breast. *South Med J*, 2006; 99(2): 164–67
8. Anavekar NS, Rozen WM, Rowe K, Murphy C: Synchronous carcinoma and lymphoma of the breast. *Clin Breast Cancer*, 2008; 8(3): 281–84
9. Benoit L, Arnould L, Collin F et al: Concurrent lymphoma and metastatic breast carcinoma in the axillary, confounding sentinel lymph-node biopsy. *Eur J Surg Oncol*, 2004; 30(4): 462–63
10. Cox J, Lunt L, Webb L: Synchronous presentation of breast carcinoma and lymphoma in the axillary nodes. *Breast*, 2006; 15(2): 246–52
11. Nathwani BN HA, Drachenberg MR: Diagnostic significance of morphologic patterns of lymphoid proliferations in lymph nodes. In: DM K (ed.), *Neoplastic Hematopathology*. Philadelphia: Lippincott Williams & Wilkins, 2001; 507–36

Conclusions

We postulate that SLN drainage could not be impaired in the presence of small lymphocytic lymphoma in the axillary lymph nodes, allowing performance of SLNB in patients with early-stage breast carcinoma and no evidence of metastatic disease in the axillary lymph nodes. However, hematological assessment would be imperative to establish the immunohistochemical type of lymphoma in these patients. Additional studies are needed to confirm that concurrent SLL does not preclude the use of SLN surgery for staging of breast cancer.