

Typical and atypical lymphatic flows in breast carcinoma



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Typical and atypical lymphatic flows in breast carcinoma

AIM: The study of sentinel lymph node has greatly increased the knowledge about lymphatic drainage in breast cancer.

MATERIAL OF STUDY: The experience of 181 patients operated for breast carcinoma in the last two years, of which 70 undergoing SLN biopsy, allowed us to highlight some peculiarities of lymphatic drainage of the breast and led us to physiological and pathological considerations about lymphatic flow in patients for breast carcinoma. We studied patients undergoing lymphoscintigraphic mapping with SLN biopsy who were candidates for breast cancer surgery.

RESULTS: Searching for SLN's location, we found that in 88.6% cases the SLN was at level I, in 8.6% it was at level II, in no case it was at level III and in 2.8% we found lymphatic drainage to the contralateral axilla.

DISCUSSION: Thanks to this dynamic study we were able to highlight a preferential subcutaneous lymphatic path from the breast parenchyma reaching the contralateral axilla, crossing anteriorly the thorax. Literature review showed CAM incidence ranges from 3.6% to 6% and can be caused by occult primary cancer of the contralateral breast, contralateral spread of breast cancer and presence of another kind of tumor.

CONCLUSIONS: The presence of contralateral axillary metastasis, although known, allowed us to scintigraphically document (for the first time) the pathway of an alternative lymph flow and to suppose the possible causes. Thanks to this observation, considerations can be drawn about clinical, pathophysiological and oncological implications, with an impact on post-operative follow-up.

KEY WORDS: Breast neoplasms, Lymphatic system, Lymphoscintigraphy, Mastectomy

Introduction

The universally acknowledged lymphatic mapping with sentinel lymph node (SLN) biopsy procedure for tumor staging showed several anatomical and physiological fea-

tures that led us to a deeper knowledge of lymphatic flow dynamics.

We studied patients undergoing lymphoscintigraphic mapping with SLN biopsy who were candidates for breast cancer surgery. We statistically evaluated the location of SLN and the possible flow paths in the cases of unusual lymphatic drainage.

The experience of 181 patients operated for breast carcinoma in the last two years, of which 70 undergoing SLN biopsy, allowed us to highlight some peculiarities of lymphatic drainage of the breast and led us to physiological and pathological considerations about lymphatic flow in affected or operated patients for breast carcinoma.

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For this study, we referred to clinical records of patients treated in the last two years in the “Francesco Durante” Department, “Umberto I” Hospital, “Sapienza” University of Rome.

This study reports our critical analysis of findings.

Material and Methods

The study includes a group of 181 patients, 2 men and 179 women, between 35 and 93 years-old, all suffering from breast cancer, admitted to the “Umberto I” Hospital in Rome, between 2012 and 2013 (Fig. 1).

Seventy patients underwent SLN biopsy and then, after definitive histologic examination, 15 have been converted to lymphadenectomy.

The procedures followed were in accordance with the ethical standards of the responsible institutional committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Searching for SLN's location, we found that in 62/70 cases (88.6%) the SLN was at level I, in 06/70 cases (8.6%) it was at level II, in no case it was at level III and in 02/70 cases (2.8%) we found lymphatic drainage

to the contralateral axilla (Fig. 2). Our results are similar to those published by Marrazzo et al. in 2014 (22), who suggested for this reason level I lymphadenectomy, when it's not possible to identify SLN location. In the 2 cases of contralateral axillary drainage we reported, it was local recurrence in patients who already underwent upper outer left quadrantectomy and ipsilateral lymphadenectomy for invasive ductal breast carcinoma (one 23 years before and one 20 years before), both treated with adjuvant radio-/chemo-therapy.

Both patients underwent radical-mastectomy for recurrent disease; the first one had clear signs of contralateral axillary metastasis (CAM) and then we performed contralateral axillary lymphadenectomy, since all preoperative exams excluded tumor presence in the other breast. The subsequent observation of another case of a patient similar to the previous led us to investigate which path the lymphatic drainage could follow to reach lymph nodes.

Even in this case, the lymphatic drainage arrived to the contralateral axilla, although histologic examination showed no lymph nodal metastasis.

Discussion and Comments

The experience of 181 patients operated for breast carcinoma in the last two years, of which 70 undergoing SLN biopsy, allowed us to highlight some peculiarities of lymphatic drainage of the breast and led us to physiological and pathological considerations about lymphatic flow in affected or operated patients for breast carcinoma.

In most of the cases (88.6%) SLN was typically localized at I level nodes, as we expected.

In a few cases (8.6%) SLN was localized at II level nodes and in our opinion it suggests that typical anatomical distinction among first, second and third level lightly diverges from what should be considered a strictly physiological classification. Indeed, unlike venous system, lymphatic system is considerably thicker and thus a variation of SLN localization is predictable. Those differences must be considered when it is not possible to identify SLN and it should not be sufficient performing a I level lymphadenectomy.

We also analyzed the two cases of contralateral axillary flow we encountered (Fig. 3). Indeed, after the observation of a first case of contralateral axillary metastasis, we were interested about the reasons that could modify the lymphatic drainage, and which paths the lymphatic flow should follow to reach contralateral axillary nodes. As known, SLN mapping is not indicated in patients with relapsed disease, therefore we only performed axillary lymphadenectomy that confirmed the presence of metastasis with the same identical features of primitive cancer¹.

Although not strictly indicated, the observation of the second case inspired us to document (by “minute by

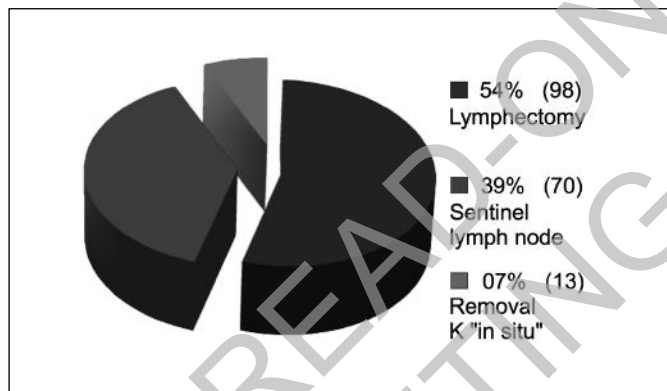


Fig. 1: Total Patients (181) and Sentinel Lymph Nodes Rate.

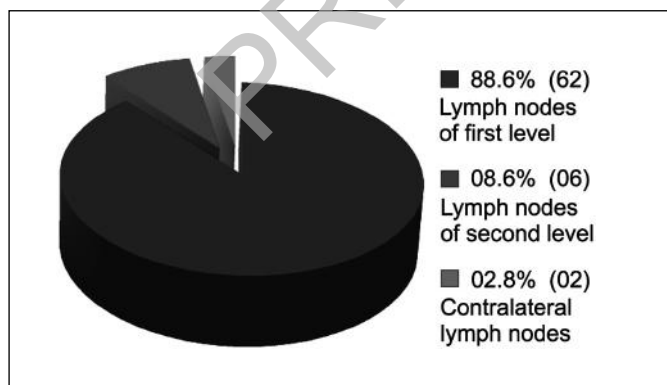


Fig. 2: Localization of the sentinel lymph node

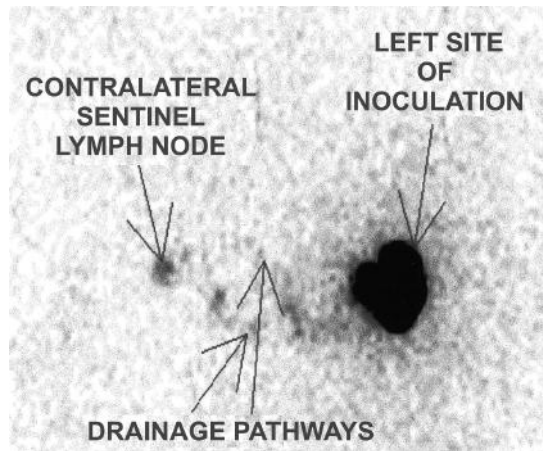


Fig. 3: Scintigraphic mapping in anterior projection showing 2 lymphatic pathways from left upper outer quadrant to SLN in right axilla

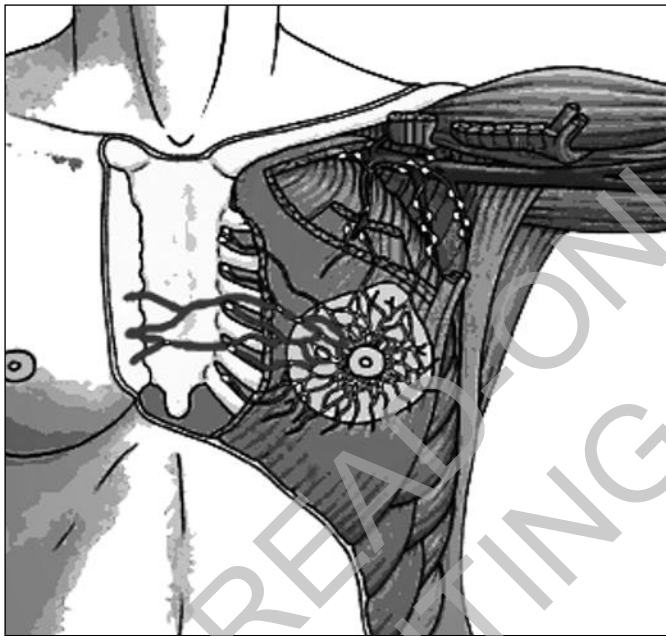


Fig. 4: It is highlighted the presence of subcutaneous lymphatic pathways that link the lymphatic network of one breast with the contralateral breast. Modified from: *Neoplasie Della Mammella*. Cosmi EV, Pinotti JA et al. SEE Editrice Firenze, 1997 pag. 79-82.

minute" scintigraphy) what was the path followed by the lymph flow to reach the contralateral lymph nodes (Fig. 3). Thanks to this dynamic study we were able to highlight a preferential subcutaneous lymphatic path from the breast parenchyma reaching the contralateral axilla, crossing anteriorly the thorax (Fig. 4).

Literature review showed CAM can be caused by:

- occult primary cancer (unrecognized cancer 0.3-1%) of the contralateral breast ^{2,4};
- contralateral spread of breast cancer ^{2,5}
- presence of another kind of tumor (e.g. cancer of thyroid, lungs, GI tract, melanomas etc.) ^{2,5};

CAM incidence ranges from 3.6% to 6% ^{2,3}, although according to Morcos et al.⁴ this range is probably overestimated, since in some studies the diagnosis was based on clinical examination only.

Surgery, radiotherapy and chemotherapy can modify common lymphatic drainage, causing the deviation of the flow on alternative pathways ^{3,5,23}, as it can occur in the internal mammary lymph nodes metastasis ^{7,11,25}. Embryologically, the breast originates from the ectodermal layer that develops organs and structures that maintain contact with the outside world (CNS, PNS, skin, hair, nails) ^{12,13}, and therefore both the breast and its lymphatic network originate from the same cell clone, which could explain the lymphatic drainage through the subcutaneous network, preferably on the ipsilateral axillary lymph nodes, more rarely in the contralateral side. There seems to be a slight prevalence of CAM that metastasizes from left breast cancer to the right axilla (14/18) ^{2,4,6,14-20} even though the two works that show the major issues did not report this data ^{5,7}.

According to Gauthier (2010) et al., Agarwal et al., (2005) and Kiluk et al. (2014), CAM should be considered as a locally advanced disease (M0) in the same way as the ipsilateral axillary lymph node metastases, even considering the possible direct cancer drainage to the contralateral lymph nodes ^{3,6,7}.

Instead, according to the TMN classification, detection of CAM should be considered as distant metastasis (M1), and then as a stage IV cancer ^{3,8}. Same orientation is shared by the NCCN 2013 guidelines.

In our records, SLN mapping never showed involvement of the supraclavicular lymph nodes and indeed, metastasis is more rarely observed in this site,

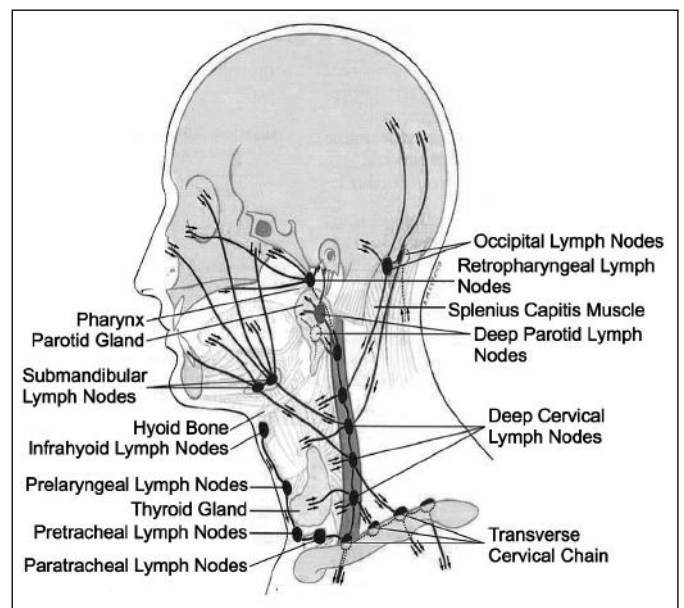


Fig. 5: Figure shows the lymphatic flow direction. Modified from: Balboni GC, Bastianini A, Brizzi E : *Anatomia umana*. Vol. I. Edi-Ermes. 2000: 592-99.

since the drainage of supraclavicular and cervical lymph node stations (Fig. 5) is mainly from top to bottom^{9,10,23}.

Metastases to the internal mammary lymph nodes, not present in our cases, have been reported in other series as 13% of cases²¹, and the main risk factors are:

- age under 35 years;
- tumor grade;
- lymphovascular invasion;
- localization of the tumor in the central or inner quadrants of the breast;
- positive axillary lymph nodes.

The lymphatic drainage of the internal mammary lymph nodes may even cross those of the contralateral chain, and already in 1987 Pasta et al.^{1,11} performed a lymphoscintigraphic study in this regard based on the experience of 11 patients undergoing mastectomy for breast carcinoma, by studying the behavior of lymph node metastases in the internal mammary chain. They already documented the possibility of deviation of lymph flow to the contralateral chain and they also emphasized the role of lymphoscintigraphy in the study of post-operative lymph node metastases from breast cancer.

Especially in patients undergoing lymphadenectomy and/or radiotherapy, due to the removing or reducing of the natural routes of lymph flow, lymph can alternatively make its way through the dermo-epidermal network, reaching the contralateral axilla^{23,24}.

Conclusions

The study of sentinel lymph node has greatly increased the knowledge about lymphatic drainage in breast cancer. The observation of a low rate of SLNs located at level II lymph node stations confirmed the difference between anatomical/surgical classification and fisiological classification.

In our opinion, the lack of SLNs located at lymph node stations of internal mammary chain and supraclavicular chain depends on anatomical and clinical reasons.

Finally, the presence of contralateral axillary metastasis, although known, allowed us to scintigraphically document (for the first time) the pathway of an alternative lymph flow and to suppose the possible causes. Thanks to this observation, considerations can be drawn about clinical, pathophysiological and oncological implications, with an impact on post-operative follow-up.

Riassunto

La pratica, universalmente riconosciuta, della ricerca e biopsia del linfonodo sentinella nella stadiazione dei tumori ha evidenziato una serie di situazioni anatomiche e fisiologiche che hanno consentito una più approfondita conoscenza del comportamento del flusso

linfatico nel soggetto sano e nel paziente affetto da neoplasia.

In particolar modo abbiamo concentrato la nostra attenzione sulle pazienti sottoposte a ricerca linfoscintigrafica del linfonodo sentinella in vista di interventi chirurgici per carcinoma mammario; abbiamo valutato statisticamente la sede in cui è stato reperito il LS e nell'eventualità di drenaggio in sedi anomale il percorso del flusso linfatico.

Si è fatto riferimento, per questo studio, alla casistica del Dipartimento di Scienze Chirurgiche dell'Università La Sapienza di Roma maturata negli ultimi 2 anni.

Lo scopo del nostro studio è stato quello di valutare statisticamente la sede del linfonodo sentinella, le possibilità di flussi linfatici in direzione non usuale e in questi casi dove, quando e perché.

Ne sono emersi riscontri degni di analisi critica e considerazioni oggetto del presente lavoro.

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References

1. Pasta V, Urciuoli P, D'Orazi V, Sottile D, Monti M, Redler A: *Contralateral axillary metastases from breast cancer and review of the literature*. Ann Ital Chir, 2014; 85(3):260-64.
2. Lanitis S, Behranwala KA, AL-Mufti R, Hadjiminas D: *Axillary metastatic disease as presentation of occult or contralateral breast cancer*. Breast, 2009; 18:225-27.
3. Gauthier T, Monteil J, Bourneton N, Jammet I: *Contralateral axillary involvement in breast cancer recurrence: Locoregional disease or metastasis?* Eur J Gynaecol Oncol 2010; 31(6): 694-96.
4. Yirmibesoglu E, Tekin E, Memis L, Yamac D, Taneri F, Sukru Erkal H: *A patient with occult breast cancer presenting with an axillary lymph node metastasis and a synchronous contralateral breast cancer*. The Breast, 2005; 14:157-62.
5. Morcos B, Jaradat I, EL-Ghanem M: *Characteristics of and therapeutic options for contralateral axillary lymph node metastasis in breast cancer*. Eur J Surg Oncol, 2011; 37(5): 418-21.
6. Agarwal A, Heron DE, Sumkin J, Falk J: *Contralateral uptake and metastases in sentinel lymph node mapping for recurrent breast cancer*. J Surg Oncol, 2005, 92(1):4-8.
7. Kiluk JV, Prowler V, Lee MC, Khakpour N, Laronga C, Cox CE: *Contralateral axillary nodal involvement from invasive breast cancer*. Breast, 2014; 23(3): 291-94.
8. NCCN Clinical Practice guidelines in Oncology: Breast cancer. Version 3. 2013.
9. Balboni GC, Bastianini A, Brizzi E: *Anatomia umana*. Vol.1. Roma: Edi-Ermes, 2000; 592-99.
10. Cosmi EV, Pinotti JA, et al.: *Neoplasie della Mammella*. Firenze: SEE Editrice, 1997; 79-82.

11. Pasta V, Trinci M, Nudo M, Monti M, Redler A, Marchesi M, Tartaglia F, Biffoni M, Marchese V, Vergine M: *Role of lymphoscintigraphy in the postoperative study of the patient operated for cancer of the breast*. Ann Ital Chir, 1987; 59(1-6): 343-50. Article in Italian.
12. Balboni GC, Bastianini A, Brizzi E: *Anatomia umana*. Vol. III. Roma, Edi-Ermes, 2000; 557-60.
13. Sandler TW: *Embriologia medica di Langman*. Padova: Piccin. 1999; 327-28.
14. Capobianco G, Spaliviero B, Dessole S, Cossu Rocca P, Cherchi PL, Ambrosini G, Meloni F, Meloni GB: *Lymph node axillary metastasis from occult contralateral infiltrating lobular carcinoma arising in accessory areola: MRI Diagnosis*. Breast J, 2007; 13(3): 305-07.
15. Carmon M, Mintz A, Hain D, Olsha O: *Clinical implications of contralateral axillary sentinel lymph nodes*. Breast, 2006; 15(2): 266-68.
16. Lim I, Shim J, Goyenechea M, Kim CK, Krynycky BR: *Drainage across midline to sentinel nodes in the contralateral axilla in breast cancer*. Nucl Med, 2004; 29(6): 346-67.
17. Barranger E, Montravers F, Kerrou K, Marpeau O, Raileanu I, Antoine M, Talbot JN, Uzan S: *Contralateral axillary sentinel lymph node drainage in breast cancer: A case report*. J Surg Oncol, 2004; 86(3): 167-69.
18. Herold CI, Gaughan EM, Lamb CC, Tung NM: *Second primary ipsilateral breast cancer with contralateral axillary involvement: a case report and literature review*. Clin Breast Cancer, 2011; 11(6): 406-08.
19. Huston TL, Pressman PI, Moore A, Vahdat L, Hoda SA, Kato M, Weinstein D, Tousimis E: *The presentation of contralateral axillary lymph node metastases from breast carcinoma: A clinical management dilemma*. Breast J, 2007; 13(2):158-64.
20. Kinoshita S, Hirano A, Kobayashi S, Komine K, Kyoda S, Takeyama H, Uchida K, Morikawa T, Nagase J, Sakamoto G: *Metachronous secondary primary occult breast cancer initially presenting with metastases to the contralateral axillary lymph nodes: Report of a case*. Breast Cancer, 2010; 17(1): 71-74.
21. Gnerlich JL, Barreto-Andrade JC, Czechura T, John JR, Turk MA, Kennedy TJ, Winchester DJ: *Accurate staging with internal mammary chain sentinel node biopsy for breast cancer*. Ann Surg Oncol, 2014; 21: 368-74.
22. Marrazzo A, Palumbo D V, Marrazzo E, Taormina P, Damiano G, Buscemi S, Buscemi G, Lo Monte AI: *Localization of sentinel lymph node in breast cancer. A prospective study*. Int J Surg, 2014; 12(Suppl 1): S162-164.
23. He ZY, Wu SG, Zhou J, Sun JY, Li FY, Lin Q, Guo L, Lin HX: *Benefit of post-mastectomy radiotherapy of the supra-/infraclavicular lymphatic drainage area in breast cancer patients*. Asian Pac J Cancer Prev, 2014; 15(14): 5557-563.
24. Tokmak H, Kaban K, Muslumanoglu M, Demirel M, Aktan S: *Management of sentinel node re-mapping in patient who have second or recurrent breast cancer and had previous axillary procedures*. World J Surg Oncol, 2014; 12(12):205.
25. Manca G, Volterrani D, Mazzarri S, Duce V, Svirydenka A, Giuliano A, Mariani G.: *Sentinel lymph node mapping in breast cancer: a critical reappraisal of the internal mammary chain*. Q J Nucl Med Mol Imaging, 2014; 58(2): 114-26.