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Original Research Article

Evaluation of sentinel lymph node biopsy after neo-adjuvant chemotherapy in locally advanced breast cancer with negative axilla

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Abstract

Sentinel lymph node biopsy (SLNB) is a procedure done for staging of tumor free axillary nodes in breast cancer patients but its use limited to early stages. Achievement of complete response after neo-adjuvant chemotherapy (NAC) evolving the reuse of SLNB in locally advanced breast cancer (LABC). Evaluation of the efficacy of sentinel lymph node biopsy in LABC patients with negative axilla after complete remission with NAC. A prospective study was carried out on 30 patients with LABC (T3-4, N0, and M0) whom received NAC. All cases underwent SLNB together with axillary clearance and surgical management of primary tumor. Identification of sentinel lymph node was achieved in 22 (62.7%) patients while not stained in 8 (37.3%) patients. The histopathology of SLNs and corresponding axillae showed that there is a statistical significance when SLNB used to evaluate the axillary status after neo-adjuvant chemotherapy with test sensitivity = 60%, specificity = 94.1%, PPV = 75%, NPV = 88.9%, and accuracy= 86.4%. After complete remission with NAC, when SLNB is negative the probability of metastasis in axilla is very low, so we can avoid axillary lymphadenectomy depending on the result of SLNB.

Keywords: Sentinel lymph node, locally advanced breast cancer, neo-adjuvant chemotherapy.

Abbreviation: ALND: axillary lymph node dissection, **CBS:** conservative breast surgery, **IDC:** infiltrating duct carcinoma, **ILC:** infiltrating lobular carcinoma, **LABC:** locally advanced breast cancer, **MRM:** modified radical mastectomy, **NAC:** neo-adjuvant chemotherapy, **SLN:** sentinel lymph node.

INTRODUCTION

The primary aims of modern breast cancer surgery are to obtain local and regional control of the cancer and gather sufficient information to make an accurate prediction of the risk of distant metastases in order to guide systemic therapy. This has traditionally been achieved by resection of the primary tumor and ALND. ALND has significant short- and long-term morbidity, the most significant being arm lymphedema (Somasundaram et al., 2017). LABC includes bulky primary breast tumor (T3-4) with any axillary lymph node status, remains an important clinical problem in developing countries and the prognosis in such tumor is often unfavorable despite aggressive treatment (Van Deurzen et al., 2009). NAC is established for treatment of locally advanced disease for down staging of an unfavorable tumor to allow less radical surgery and to increase the rate of conservative breast

surgery (CBS) (Smith, 2012). In early breast cancer there is no doubt that sentinel lymph node biopsy is the standard surgical procedure for staging of clinically tumor-free regional nodes (Kumar et al., 2012). However SLNB in locally advanced breast cancer still a matter of controversies (Manca et al., 2016). The aim of this work is to evaluate the sentinel lymph node biopsy after neo-adjuvant chemotherapy in locally advanced breast cancer with negative axilla so that we can in future reduce the unnecessary ALND.

PATIENT AND METHODS

The study was conducted at surgical oncology unit of Al-Azhar university hospital from February 2016 to May 2017. The study included 30 patients having LABC and treated by NAC. All patients agreed to perform sentinel lymph node mapping with the surgical management of breast cancer in form of modified radical mastectomy (MRM) or CBS.

Exclusion criteria

- Early breast cancer T1-T2
- Clinically positive axilla.
- Previous axillary surgery.
- Sensitivity to dye.

All patients underwent 6 cycles of neo-adjuvant chemotherapy (Anthracycline-based). All patients were subjected to complete medical history and clinical examination to assess the residual breast tumor and axillary status. At least 3 weeks after last dose of chemotherapy all patients completed their management by surgery in form of mastectomy or quadrantectomy with axillary dissection and SLN mapping.

Technique of SLN identification

- Thirty minutes before anesthesia the patient is subjected to skin sensitivity test for the blue dye in contralateral arm.
- Immediately after anesthesia and before scrub, 5cm of Isosulphane blue is injected in and around the site of primary tumor.
- The first step after mastectomy or quadrantectomy is identification of axillary vein and inter-costo-brachial nerves. Visualization of small lymphatic channels requires good Exposure and a bloodless field, so as to avoid disruption of the draining pathway of the blue dye into the SLN and leakage of the Blue dye, which will stain the surrounding tissues, compromising the detection of a blue lymph node.
- Detection of sentinel lymph nodes (blue stained) and their location:
  - Above or below the axillary vein.
  - Its relation to inter-costo-brachial nerves.
  - Medial or lateral to subscapular vessels.
  - Belong to which group of axillary LN.
- After detection of blue stained lymph node, excision of this node is done (sample No.1) as a sentinel node.
- According to the identification of SLN the cases will be classified into two groups: group A in which the SLN stained (identified) while in group B the SLN not stained and not identified.
- Completion of axillary clearance and all specimens to be send for histo-pathological examination.

All patients were observed in surgical ward, antibiotic covering and analgesics according to needs. Complications were recorded and non-complicated patients discharged 2 day post-operative.

RESULTS

Table (1) shows the clinical data of patients. The median age of studied cases was 51.7 years (range 39 - 65), four of them were diabetics, six were hypertensive, and two of them have positive family history for breast cancer. Infiltrating duct carcinoma (IDC) was the commonest diagnosis 86.6% while rest of cases was infiltrating lobular carcinoma (ILC). As regard the site of primary tumor, 9 patients (30%) had retro-areolar masses, 7 patients (23.3%) had masses medial to areola, while 14 patients (46.7%) had masses in outer quadrants. All cases selected as locally advanced breast tumors T3 in 19 cases (63.3%) and T4 in 11 cases (36.7%), but in all cases the axillae were clinically free and no systemic metastasis.

During surgical management of studied patients twenty-one cases (70%) underwent MRM, and nine cases (30%) underwent CBS. SLN identification was achieved in 22 cases (group A) (73.3%), while not stained in 8 cases (group B) (26.7%). In all patients axillary clearance was done. As regard the site of SLN (group A); 16 of stained nodes (72.7%) were located in pectoral group within one cm above or below inter-costo-brachial nerve, the remaining stained nodes (27.3%) located away from pectoral group (Table 2).

Table 3 shows the histo-pathological analysis of SLN and axilla. In group A (22 cases) there was metastasis in four SLN (18.2%) three of them associated with positive axillary metastasis. The total metastasis in the axillary LN was found in 6 cases (20%), 5 of them in group A of patients (22 stained SLN), while the other one metastasis occurred in group B.

Statistical analysis of the results of histopathology of SLNs and corresponding axillae in group A of patients showed in Table 4. There is a statistical significance when SLNB used to evaluate the axillary status after neo-adjuvant chemotherapy with test sensitivity = 60%,

Table 1. Shows the clinical and pathological data of all cases

Age	**Mean ± SD** **51.7 ± 8.1**	**Range** **39 - 65**
	Number (30)	**Percentage**
History		
DM	4	13.3%
HTN	6	20%
Family history of breast cancer	2	6.7%
Stage		
T3	19	63.3%
T4	11	36.7%
N0	30	100%
M0	30	100%
Site		
Retro-areolar	9	30%
Medial quadrants	7	23.3%
Lateral quadrants	14	46.7%
Pathology		
IDC	26	86.6%
ILC	4	13.4%

Table 2. Shows the operative data of studied patients

	No.	**%**
Surgical treatment		
MRM	21	70
CBS	9	30
SLN identification		
Stained (group A)	22	73.3
Non-stained (group B)	8	26.7
Site of stained SLN (group A)		
Pectoral	16	72.7
Non-pectoral	6	27.3

Table 3. Shows the result of histo-pathological analysis of SLN and axilla

	No.	**%**
Metastasis in SLN (22 cases)		
+ve	4	18.2
-ve	18	81.8
Metastasis in axilla (30 cases)		
Group A (22 cases)	5	16.7
Group B (8 cases)	1	3.3
Total	6	20

Table 4. Show the relation between metastasis in group A and their corresponding axillae

	Metastasis in axilla of 22 stained SLN			**P value**
Metastasis in 22 stained SLN	**Present**	**Absent**	**Total**	
Present	3(13.6%)	1(4.5%)	4(18.2%)	<0.01*
Absent	2(9.1%)	16(72.7%)	18(81.8%)	
Total	5(22.7%)	17(77.2%)	22(100.0%)	

*Statistically significant at $p<0.05$

specificity = 94.1%, PPV = 75%, NPV = 88.9%, and accuracy= 86.4%.

DISCUSSION

The most precise prognostic indicator for progression of primary breast cancer is lymph node involvement. SLNB concept suggests removal of the single first node draining the tumor lymph. After SLNB was found successful for staging of melanoma it is used for staging of breast cancer. Early results confirmed that the method was reliable, and patients were pleased with the mild degree of post-surgical morbidity and short hospital stay.

The aim of this study is to evaluate the accuracy of SLNB in locally advanced breast cancer after NAC with clinically impalpable axillary lymph nodes.Among the 30 patients who underwent sentinel lymph node mapping, it was successfully detected in 22 cases with a detection rate of 73.3%. The patients were classified according to the site of the harvested sentinel lymph node into 2 groups where 16 cases (72.7%) found below the pectoralis minor and 6 cases (27.3%) were detected away from the pectoralis minor. Comparing the results of our study to the results of Simpson et al, in 2014 where they reported overall success rate of 94.7% in identifying the sentinel node while in a previous study by the same author, they reported a rate of 90% for SLN identification with methylene blue dye (Simpson et al., 2014). In 2013, Jeffrey et al, stated that SLN mapping with Methylene blue is as good as SLN mapping with Isosulfan blue and is much cheaper. Addition of radio-colloid mapping to blue dye does not achieve a sufficiently higher identification rate to justify the cost (Jeffrey et al., 2013).

Axillary dissection of 22 patients (group A) with blue sentinel nodes showed that +ve axillary nodes for malignant cells existed in 5 (22.7%) patients and SLN wasonlypositive in 3 (13.6%) of these patients (true +ve) with false –ve result 9.1%.The rate of false-negative results best defines the accuracy of sentinel lymph node biopsy. If a sentinel node which tests negative for tumor cells at histologic examination is removed while a tumor-positive lymph node remains in the axilla, the disease will be under staged, leaving the patient at risk both for local and regional recurrence of disease and for metastasis. A false-negative rate of 5% or less is mentioned frequently in surgical literature as a goal for surgeons performing SLNB**.** In this study, false negative results was seen in 2 (9.1%) patients which is approximately near to those obtained by the meta-analysis of Geng et al. 2016,where the collective false negative rates were 6% (Geng et al., 2016).

The failure rate in this study was 26.7% representing the nodes that failed to take blue dye. The reason was that these 8 cases were in an advanced stage in which the malignant cells obstruct the lymphatic channels and this prevents the dye from reaching the nodes in spite of being impalpable during clinical examination. Compared with another study by Mathline et al, in 2009, whom stated that the presence of metastatic disease in several axillary nodes and no SLN was found implies that they were poorly selected to begin with and that failure to identify was probably due to failure of the SLN to take up the dye rather than failure of technique. Routine preoperative sonographic assessment of axillary nodes has the potential to reduce SLN identification failure for this reason if SLNB is restricted to sonographically negative rather than clinically negative cases (Mathelin et al., 2009).

CONCLUSION

After complete remission with NAC we can use SLNB for prediction of axillary status. When SLNB is negative the probability of metastasis in axilla is very low, so we can avoid axillary lymphadenectomy.

Conflicts of Interest

The author(s) indicated no potential conflicts of interest.

REFERENCES

Geng C, Chen X, Pan X, Li J (2016). The Feasibility and Accuracy of Sentinel Lymph Node Biopsy in Initially Clinically Node-Negative Breast Cancer after Neoadjuvant Chemotherapy: A Systematic Review and Meta-Analysis. PLoS One. Sep 8; 11(9):e0162605. doi: 10.1371/journal.pone.0162605.

Jeffrey M, Christopher SPV, Emil K (2013). Sentinel lymph node biopsy for breast cancer using methylene blue dye manifests a short learning curve among experienced surgeons: a prospective tabular cumulative sum (CUSUM) analysis.BMC Surgery.; 9:2.

Kumar A, Puri R, Gadgil PV, Jatoi I (2012). Sentinel lymph node biopsy in primary breast cancer: window to management of the axilla. World J Surg. Jul; 36 (7): 1453-9. doi: 10.1007/s00268-012-1635-8.

Manca G, Rubello D, Tardelli E, Giammarile F, Mazzarri S, Boni G, Chondrogiannis S, Marzola MC, Chiacchio S, Ghilli M, Roncella M, Volterrani D, Colletti PM (2016). Sentinel Lymph Node Biopsy in Breast Cancer: Indications, Contraindications, and Controversies. Clinical Nuclear Medicine. Feb; 41(2): 126–33 doi: 10.1097/RLU.0000000000000985.

Mathelin C, Croce S, Brasse D, Gairard B, Gharbi M, Andriamisandratsoa N, Bekaert V, Francis Z, Guyonnet JL, Huss D, Salvador S, Schaeffer R, Grucker D, Marin C, Bellocq JP (2009). Methylene blue dye, an accurate dye for sentinel lymph node identification in early breast cancer. Anticancer Res. Oct; 29 (10): 4119-26.

Simpson PT, Reis-Filho JS, Gale T, Lakhani SR (2014). Molecular evolution of breast cancer. J Pathol Jan; 205 (2): 248-54.

Smith BD (2012). Using chemotherapy response to personalize choices regarding locoregional therapy: a new era in breast cancer treatment? J Clin. Oncol. Nov; 30 (32):3913-5. doi: 10.1200/JCO.2012.44.4539.

Somasundaram SK, Chicken DW, Keshtgar MR (2017). Detection of the sentinel lymph node in breast cancer, Br Med Bull.; 84: 117–31.doi: 10.1093/bmb/ldm032.

Van Deurzen CH, Vriens BE, Tjan-Heijnen VC, van der Wall E, Albregts M, van Hilligersberg R, Monninkhof EM, van Diest PJ (2009). Accuracy of sentinel node biopsy after neoadjuvant chemotherapy in breast cancer patient: a systematic review. Eur J cancer Dec; 45: 3124-30. doi: 10.1016/j.ejca.2009.08.001.