ORIGINAl Article

Sentinel Lymph Node Biopsy Using Methylene Blue Dye in Early Breast Cancer. Is It Truly Reliable?

Mohamed Zaazou,1 Khaled Mahran,2 Ihab Merhem,1 Ashraf Abdel Azeem2

1General Surgery Department, Misr University for Science and Technology (MUST), 6th of October, 2General Surgery Department, Minia University, Minia, Egypt

Correspondence to: Mohamed Zaazou, Email: mzaazou@hotmail.com

Abstract

Aim: Current literature has suggested that sentinel lymph node biopsy (SLNB) may replace axillary dissection as the nodal staging procedure of choice in early breast cancer. The aim of this study is to evaluate the effectiveness and accuracy of SLNB using methylene blue dye in predicting axillary nodal status in early breast cancer with clinically impalpable axillary lymph nodes.

Methods: In the period between May 2006 and April 2009, 94 patients with early breast cancer and clinically impalpable axillary lymph nodes, underwent SLNB using methylene blue dye followed by completion of axillary dissection in the same setting after taking a written consent from the patients.

Results: Of included 94 patients, SLNB was successful in 86 (91.5%). Accuracy of SLNB was 95.3%, sensitivity was 88.2%, false negative rate was 11.8%, negative predictive value was 92.8% and rate of metastatic disease to sentinel nodes only, without other nodal affection, was 26.5%.

Conclusion: SLNB using methylene blue dye is an accurate predictor of axillary nodal status in women with early breast cancer.

Keywords: Lymphatic involvement, breast malignancy, axillary dissection

INTRODUCTION

The histological status of the first lymph node in progressive involvement of axillary nodes by tumor cells is representative of all the other axillary nodes; it is the rationale for adoption of the idea of sentinel lymph node biopsy (SLNB).1,2 In 1994, the technique of SLNB has been introduced as an alternative to more extensive node dissection for staging breast cancer. Since that time, there is increasing evidence suggesting that SLNB can be performed in early breast cancer in patients with clinically impalpable axillary LN and if it is negative, axillary lymph node dissection should be avoided.3-5 So, SLNB is accepted as a valid technique for axillary staging in clinical T1-2, N0 breast cancer.6-7 This was approved in the Consensus Conference in Philadelphia, 2001 due to its high sensitivity and accuracy in predicting axillary lymph node affection.5 The randomized trial comparing SLNB and complete axillary dissection in breast cancer patients confirmed the accuracy of SLNB in predicting the status of the axillary lymph nodes without a significant risk of relapse of disease in the axilla,4 in addition to decreased risk of postoperative morbidity when
compared with extensive axillary lymph node dissection. The aim of this study is to evaluate the effectiveness and accuracy of SLNB in early breast cancer with clinically impalpable axillary lymph nodes using methylene blue dye.

**PATIENTS AND METHODS**

This study was conducted at the university hospitals of both MUST (Misr University for Science and Technology Hospital) and Minia Universities in the period between May 2006 and April 2009. This study included 94 female patients. Their age ranged from 38-57 years old with mean age of 48 years. Informed consent for sentinel lymph node biopsy, axillary clearance and lumpectomy and using the methylene blue dye was obtained from each patient. The criteria for inclusion in the study were a histologically proved diagnosis of T1 or T2 breast cancer depending on FNAC plus clinical and mammographic data with clinically node negative axilla. Patients with any of the following criteria were excluded from this study: locally advanced cancer (T3-T4), clinically palpable axillary lymph nodes, previous axillary surgery, previous chemotherapy administration and patients with ductal carcinoma in situ with extensive in situ component proved by postoperative histopathology or multicentric lesions.

Technique of SLNB (Figs 1-3).

The sentinel node biopsy was performed in the operative room using the methylene blue dye technique only without the adjunctive radioisotope labeling with gamma probe. Five ml of locally made methylene blue dye were infiltrated peritumorally within 0.5 cm, or subcutaneously within 0.5 cm of the tumor in palpable cancers followed by 5 minutes of massage and 20 minutes later surgery was performed. During surgery, the axilla was searched for the nodes which were stained by the dye and dissected separately through separate incision. All blue stained nodes at any level were excised and sent in a separate pot labeled sentinel nodes before completion of the axillary dissection and lumpectomy. Specimens were sent for histopathological assessment using H&E staining. A SLNB was considered successful when there was no remaining visible blue staining nodes in the axilla. Most of our patients have the tumor in the upper outer quadrants. Table 1. Tumor size varied from 1.5 cm to 4 cm with an average of 2.6 cm. Prior to surgery patients were subjected to metastatic workup and proved absence of distant metastasis.

RESULTS

Of the 94 patients who met the inclusion criteria, the overall successful SLNB rate was 91.5% (86 of 94) in which the sentinel node was successfully identified by blue dye. The pathology of the breast lesion in those patients is shown in Table 2. The results for the 86 patients in whom sentinel node biopsy was successful comparing the results of the SLNB with those of axillary dissection are shown in Table 3. The accuracy of the sentinel node as an indicator of axillary status was 95.3% (82 of 86); the sensitivity was 88.2% (30 of 34); the false negative rate was 11.8% (4 of 34 histologically positive nodes); the negative predictive value was 92.8% (52 of 56). The rate of metastatic disease to sentinel nodes only, without other nodal affection, was 26.5% (9 of 34).
Table 1. Tumor site.

<table>
<thead>
<tr>
<th>Site</th>
<th>No of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left upper outer quadrant</td>
<td>37</td>
<td>39.4%</td>
</tr>
<tr>
<td>Left upper inner quadrant</td>
<td>7</td>
<td>7.4%</td>
</tr>
<tr>
<td>Left lower outer quadrant</td>
<td>13</td>
<td>13.8%</td>
</tr>
<tr>
<td>Right upper outer quadrant</td>
<td>25</td>
<td>26.6%</td>
</tr>
<tr>
<td>Right upper inner quadrant</td>
<td>3</td>
<td>3.2%</td>
</tr>
<tr>
<td>Right lower outer quadrant</td>
<td>9</td>
<td>9.6%</td>
</tr>
</tbody>
</table>

Table 2. Pathology of the breast lesion in the 94 patients.

<table>
<thead>
<tr>
<th>Pathological type</th>
<th>No of cases</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>Ductal carcinoma</td>
<td>66</td>
<td>70.2%</td>
</tr>
<tr>
<td>Lobular carcinoma</td>
<td>19</td>
<td>20.2%</td>
</tr>
<tr>
<td>Mixed ductal and lobular carcinoma</td>
<td>9</td>
<td>9.6%</td>
</tr>
<tr>
<td>Total</td>
<td>94</td>
<td>100%</td>
</tr>
</tbody>
</table>

Table 3. Results for 86 patients with successful sentinel node biopsy.

<table>
<thead>
<tr>
<th>Sentinel nodes</th>
<th>Axillary nodes</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Negative</td>
<td>Positive</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Number of patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30</td>
<td>9</td>
<td>21</td>
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<td></td>
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<tr>
<td>56</td>
<td>52</td>
<td>4</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>86</td>
<td>61</td>
<td>25</td>
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</tbody>
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DISCUSSION
The concept of full axillary clearance is now not accepted for many patients with small breast cancers, and then several issues are required to ensure the maximum efficiency of limited axillary surgery.\(^{10}\) SLNB is a well-established, minimally invasive method of axillary staging in patients with breast cancer with clinically negative axillary LN.\(^{11}\) SLNB in early breast cancer aims at identifying as many truly node negative patients as possible, sparing them unnecessary axillary dissection and related morbidity.\(^ {12,13}\) Our findings support the hypothesis that the sentinel node is an accurate predictor of axillary nodal status in women with early breast cancer. In this study, using blue dye was successful in revealing a sentinel node in 91.5% of cases which is comparable to previous studies reporting rates of sentinel node identification with methylene blue dye ranging from 83% to 93%.\(^ {14-19}\) The remaining patients who did not show dye in the SLN showed involvement of these nodes with malignant deposits which also affect non-sentinel axillary nodes. This may explain that they did not show any dye within. The rate of false-negative results defines the accuracy of SLNB as if the negative sentinel node is removed while the positive node remains in the axilla, the disease will be understaged, leaving the patient at risk for recurrence. When successfully identified, SLNB accurately predicts axillary node status 95.3% (82 of 86) with false negative results in 11.8% (4 of 34), this is comparable with other series reporting 0-17% false negative results.\(^ {20,21}\) These false negatives may be due to the inexperience of surgeons with SLNB procedure, as well as a result of extensive tumor infiltration of the primary node draining the tumor. Patients who will gain therapeutic benefit from axillary dissection are those with nodal metastases. In our study, 52 of 86 (60.5%) successful sentinel node biopsies had histologically negative nodes. These patients could have been spared a complete axillary dissection. This agreed with Fenaroli et al.\(^ {22}\) who reported that SLNB can spare axillary dissection in approximately half of cases of early breast cancer This result further clarifies the advantage of SLNB in that it allows tailoring therapy according to the extent of the patient’s disease.

We concluded that SLNB using methylene blue dye is an accurate predictor of axillary nodal status in women with early breast cancer. So, in cases of -ve SLNB using methylene blue saving axilla can be decided safely while in +ve cases axillary dissection is completed.

REFERENCES


