

Methylene blue for sentinel lymph node localisation in breast cancer surgery: Experience of RIPAS Hospital

Sonal TRIPATHI ¹, Hani TRASIL ¹, Pemasiri Upali TELISINGHE ²

¹ Department of Surgery and ² Department of Pathology, RIPAS Hospital, Brunei Darussalam

ABSTRACT

Introduction: Axillary lymph node dissection (ALND) is a standard procedure in the management of breast cancer for diagnosis of axillary node metastasis and for local control. The aim of this study was to investigate the ease and the effectiveness of using methylene blue dye in the localisation of sentinel lymph node (SLN) and biopsy (SLNB) in patients undergoing surgery for breast cancer at RIPAS Hospital. **Materials and Methods:** Twenty-five patients with confirmed fine needle aspiration cytological diagnosis of breast cancer, who were undergoing planned mastectomy and axillary node clearance, were included in the study. Four to five milliliters of methylene blue dye was injected into the peritumour area 20 to 30 minutes preoperatively before surgical incision was made. All SLNs were submitted for intra-operative frozen section analysis. All patients underwent mastectomy and Level II axillary clearance. **Results:** Methylene blue dye staining and localisation of SLNs were positive in 22 (88%) patients, out of which 10 (45.45%) patients had SLN which were positive for metastasis. In three patients (12%), the dye failed to reach the axilla with one patient having micro-metastasis in the axillary lymph nodes. The mean duration to SLN harvesting was 20 min (range 15 to 25 min) after injection of the methylene blue. Complications included blue discolouration of urine (28%), post-operative fever (4%), tattooing near the scar (4%) and a small area of skin necrosis near the scar (4%). **Conclusions:** In our setting, SLNB using methylene blue dye is also an effective method for accurately identifying SLNs in breast cancer patients and provide an accurate pathological staging without having to do a formal axillary clearance.

Keywords: Axillary nodes, breast carcinoma, lymph nodes, sentinel node biopsy

INTRODUCTION

Breast cancer is the number one cancer among females, comprising 10.9% of all can-

cers among women, and is the most common type of non-skin cancer. ¹ It is the fifth most common cause of cancer death worldwide. ¹ Breast cancer is about 100 times more common in women than in men.

Correspondence author: Sonal TRIPATHI
Department of Surgery,
RIPAS Hospital, Bandar Seri Begawan BA 1710,
Brunei Darussalam.
Tel: +673 8660850 or +673 2450449
E mail: sonal230167@yahoo.com

Axillary lymph nodes are the most

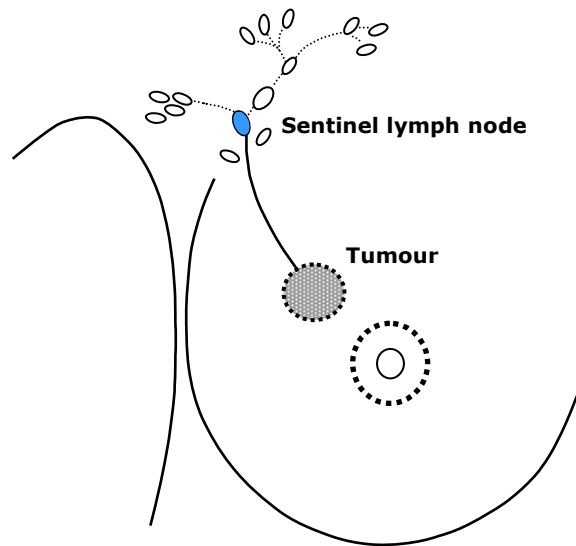


Fig. 1: Sentinel lymph node (shaded blue) and lymphatic drainage of breast tumour.

frequent site of metastasis from breast cancer. Axillary lymph node dissection (ALND) is a standard procedure performed in the management of breast cancer, and remains the best method to determine if axillary lymph node metastasis is present.²

Recent data supports the use of adjuvant chemotherapy regardless of axillary node status and ALND may not be necessary in all patients, particularly in patients with early breast cancer.^{3,4} Only patients with axillary metastasis benefit from undergoing ALND. The number of patients in this group is however decreasing, due to screening programs and also as the size of primary tumour has been progressively decreasing over the last two decades due to better awareness, early presentations and detection. Many patients therefore still undergo unnecessary axillary dissection, which carries substantial morbidity.

The sentinel lymph node (SLN) is the first node to receive the lymphatic drainage and metastasis from the breast (Figure 1). It

is usually an axillary node, and most often is in the central group (Level I). Histological status of the SLN is thought to represent the status of the entire axillary node basin. Failure to detect metastasis in the SLN accurately predicts the negativity of the remaining axillary nodes and mitigates the need for more extensive axillary dissection.^{5,6} But if SLN biopsy (SLNB) is positive, then complete ALND should be carried out.²

This study was conducted at RIPAS hospital (March 2008 to February 2009) with the aims of assessing: a) accuracy of methylene blue dye in identifying the SLN, b) time taken to harvesting of the SLN and, c) complications of methylene blue use. At the same time, this study was carried out to assess the ease of using methylene blue in someone who had not previously used this technique.

MATERIALS AND METHODS

We selected patients with confirmed carcinoma of the breast (tumour size not more than four cm) and who were scheduled for

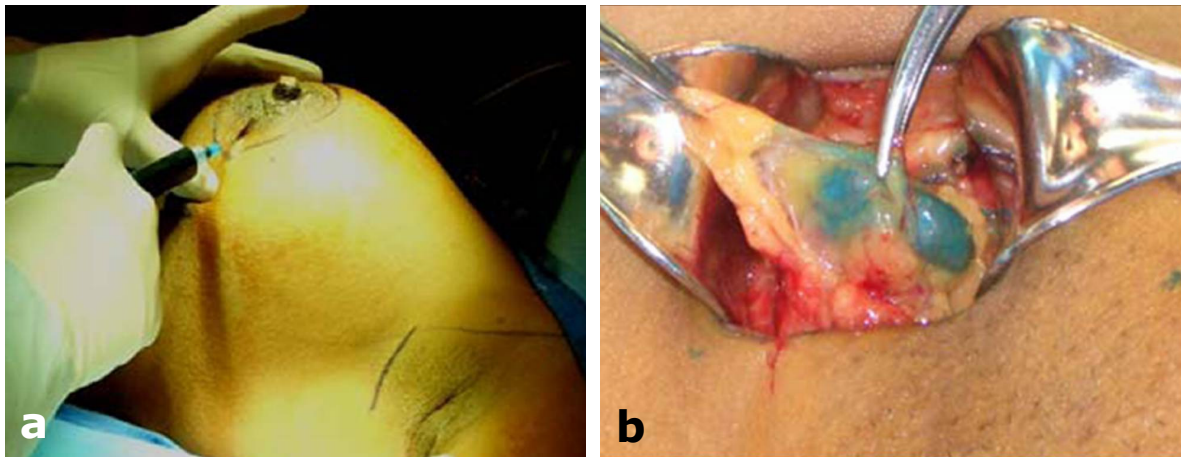


Fig. 2: a) Peri-tumoural injection of methylene blue, b) localisation of the sentinel lymph node that is stained blue by the methylene blue dye.

mastectomy or breast conserving surgery with ALND. We excluded patients with stage IV disease or locally advanced tumour, patients with palpable lymph nodes and patients with high perioperative risks. All patients were informed of the procedure and consent was taken prior to surgery.

Procedure: All patients received intravenous hydrocortisone (200mg) and piriton (Chlorpheniramine maleate BP, Pirimat ® Duopharma, Malaysia) 1ml (10mg), 20 minutes prior to methylene blue injection. One percent methylene blue (4 to 5ml) was injected around the tumour or around the areola (Figure 2a), followed by hand massage in circular motion for three to five minutes. Axillary dissection was performed first and the SLN was identified by tracing the dye to the deep blue coloured node (Figure 2b) at Level I (below and lateral to pectoralis minor). We harvested a minimum of two to three lymph nodes in each patient. The time taken to SLN harvesting was carefully noted. All SLNs were sent for frozen section and all patients underwent complete ALND irrespective of frozen section results. Tumour size was noted during surgery and was confirmed with detailed

measurement of the resected specimens.

Continuous data were presented as mean \pm standard deviation.

RESULTS

The most commonly affected site of the breast was the outer upper quadrant (32%, n=8) followed by the inner upper quadrant (24%, n=6), the center (20%, n=5), the lower outer quadrant (16%, n=4) and the inner lower quadrant (8%, n=2).

The mean duration to SLN harvesting was 20 minutes (range 15 to 25 minutes) after injection of the methylene blue. The mean number of lymph nodes harvested per patient was 2.5 (range 1 to 4) nodes. In 13 (52%) patients, the harvested nodes were negative for malignancy, while in nine (36%) patients, lymph nodes were positive for malignancy on frozen section. There were three (12%) cases who failed SLNB and the reasons for failure included, previous breast surgeries in two patients and in one patient, the dye failed to reach the axilla.

On histological examination, in 12

patients all the harvested SLNs and other axillary nodes were negative for malignancy. In six patients, the SLNs were positive for malignancy but had negative non-SLN or axillary nodes. Four patients were positive for both SLN and axillary nodes. One patient had micro-metastasis on frozen section which was negative for other nodes. The resected tumours were categorised into T-1 in nine, T-2 in 12 and T-3 size tumours in four patients respectively.

Complications included blue discolouration of urine (28%), post-operative fever (4%), tattooing near the scar (4%) and a small area of skin necrosis near the scar (4%). None of the patients had any primary or delayed hypersensitivity reaction to methylene blue dye.

DISCUSSION

Lymphatic mapping and biopsy of the SLN as a method for pathologically staging breast cancer has been extensively evaluated over the last decade. However, there is no previous study assessing the role of SLN in our local setting. SLN biopsy has the potential to drastically reduce the incidence of morbidity related to surgical staging of the regional lymph nodes in women with breast cancer.^{4, 7, 8} However, not every patient can undergo SLNB. Contraindications include locally advanced breast cancer, palpable lymph node, multi-focal breast cancer, previous breast surgery or axillary radiotherapy, allergies to dye and pregnancy.²

For most patients a single mapping agent, in an experienced hand, either a visual tracer or isotope will suffice in providing concise nodal staging.⁸ But for patients with me-

dial quadrant lesions, which can drain to the internal mammary chain first, a radio-labeled tracer has added advantage as it can identify tumour cell migration into the internal mammary chain. We used methylene blue dye for study because it is safe, easily available and relatively cheap and is well supported by literature.^{5, 8, 9, 10} Visual tracer is useful where isotope facilities are not available or when radiography and radio isotope is contraindicated i.e. pregnancy.

Patients undergoing SLNB should be informed that there is a less than 10% chance that the results of the SLN biopsy can be inaccurate (false negatives), which can be due to skip lesions or due to faulty technique. We should also be aware that the SLNB is not an alternative to axillary dissection in breast cancer. SLNB has been reported to miss cancerous cells in less than nine percent of cases, however these patients did not develop a new cancerous tumour during follow-up.¹¹ It has also been shown that patients who had SLNB experienced significantly less swelling and numbness compared to standard lymph node removal.¹²

In our study SLN identification rate was 88% and this improved to 95.7% if we excluded the two patients who had previous breast surgery. Previous surgery is known to cause damage or disrupt the lymphatic channel. In one patient, we failed to identify the SLN, as the dye had failed to reach the axilla. This was attributed to improper injection techniques. Our time to harvest the nodes was reasonable and this improved with each successive case.

In conclusion, we showed that use of

methylene blue dye to identify the SLN was easy and can be easily learned. Our results are comparable to what has been reported. The total number of nodes and time taken to harvest the nodes were within standard limit. We did not experience any major complications with the use of methylene blue.

REFERENCES

- 1:** GLOBOCAN 2008 Cancer Fact Sheet. Breast cancer incidence and mortality worldwide in 2008 summary. Available from <http://globocan.iarc.fr/factsheets/cancers/breast.asp> (Accessed 15th August 2010).
- 2:** Schwartz GF. Clinical practice guidelines for the use of axillary sentinel lymph node biopsy in carcinoma of the breast: current update. *Breast J.* 2004; 10:85-8.
- 3:** Haigh PI, Hsueh EC, Giuliano AE. Sentinel lymphadenectomy in breast cancer. *Breast Cancer* 1999; 6:139-44.
- 4:** Reitsamer R, Peintinger F, Prokop E, Rettenbacher L, Menzel C. 200 Sentinel lymph node biopsies without axillary lymph node dissection--no axillary recurrences after a 3-year follow-up. *Br J Cancer.* 2004; 90:1551-4.
- 5:** East JM, Valentine CS, Kanchev E, Blake GO. 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 Surg.* 2009 Jan 27; 9:2.
- 6:** Veronesi U, Paganelli G, Galimberti V, et al. Sentinel-node biopsy to avoid axillary dissection in breast cancer with clinically negative lymph-nodes. *Lancet* 1997;349:1864-7.
- 7:** Takei H, Kurosumi M, Yoshida T, et al. Current trends of sentinel lymph node biopsy for breast cancer— a surgeon's perspective. *Breast Cancer.* 2007; 14:362-70.
- 8:** Simmons R, Thevarajah S, Brennan MB, Christos P, Osborne M. Methylene blue dye as an alternative to isosulfan blue dye for sentinel lymph node localization. *Ann Surg Oncol.* 2003; 10:242-7.
- 9:** Thevarajah S, Huston TL, Simmons RM. A comparison of the adverse reactions associated with isosulfan blue verses methylene blue dye in sentinel lymph node biopsy for breast cancer. *Am J Surg.* 2005; 189:236-9.
- 10:** Winchester DJ. A better blue dye. *Ann Surg Oncol.* 2003; 10:208-9.
- 11:** Krontiras H, Bland KI. When is sentinel node biopsy for breast cancer contraindicated? *Surg Oncol.* 2003; 12:207-10.
- 12:** McLaughlin SA, Wright MJ, Morris KT, et al. Prevalence of lymphedema in women with breast cancer 5 years after sentinel lymph node biopsy or axillary dissection: objective measurements. *J Clin Oncol.* 2008; 26:5213-9.