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Sentinel Lymph Node Biopsy Using a Single-Dye Technique in a Cancer Center of North-East India

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Abstract

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Background Sentinel lymph node (SLN) is the first node to receive the drainage directly from a tumor. SLN biopsy can be done in lieu of a formal lymphadenectomy in selected clinically node-negative cancers and minimizes morbidity compared with the latter.

Methods This prospective study was done in patients with operable clinically node-negative breast cancer, penile cancer, and malignant melanoma of extremities in a cancer center of North-east India from January 2019 to December 2019. All the patients underwent formal lymph nodal dissection after the SLN biopsy. Besides intra-operative frozen section study of the sentinel node(s), all the specimens, including the sentinel node(s), were subjected to paraffin section histopathology.

Results SLN was identified successfully in 96% of patients. Mean number of sentinel node(s) dissected was 2.3. Study of SLN biopsy with methylene blue dye for staging was done with 100% sensitivity and 95.3% specificity. The SLN procedure was able to negatively predict the drainage nodal basin in 100% with an overall accuracy of staging of 96.5%. The true-positive rate noted was 88.8%, and the false-positive rate was 4.6%.

Conclusions SLN using a single-dye technique reliably identifies a sentinel node. This procedure can be safely adopted in patients with node-negative cancers as mentioned above to pathologically study the drainage basin.

Keywords

- breast cancer
- melanoma
- methylene blue
- penile cancer
- sentinel node
- single-dye technique

Introduction

Sentinel lymph node (SLN) biopsy has become a standard of care for regional lymph node staging of many solid tumors. This technique is based on the hypothesis of stepwise distribution of malignant cells in the lymphatic system. The absence of tumor cells in the first lymph node(s) in the lymphatic drainage of a tumor would indicate the absence of further spread in the regional lymph node basin(s).The SLN concept was initially proposed in 1960 and is currently considered among the most important advances in cancer therapy.[1] After many years of research on various types of malignancies, SLN biopsy has become the standard of care in the treatment of melanoma, breast, vulvar, and cervical cancer, sparing many patients from the morbidity associated with a formal lymphadenectomy. SLN biopsy can be a useful tool for minimizing the risks and morbidity associated with surgery.[2]

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Notwithstanding the advances in imaging that can often identify suspicious nodes in the drainage lymphatic basin, false-negative findings and failure to detect occult metastasis are common.[3] Thus reliance on histological examination of removed lymph nodes is the most accurate method for assessing spread of disease to the lymph nodes.

In 1992, Morton and colleagues[4] reported a technique for lymphatic mapping and sentinel node biopsy (SNB) in clinically node-negative melanoma patients. The concept of SNB was first introduced in penile cancer by Cabanas. Other authors have reported the results of sentinel node mapping for breast cancer using blue dye[5,6] or radioisotope,[7,8] or both.[9,10] These studies suggest that SNB may be an accurate alternative staging procedure for patients with clinically node-negative breast cancer. We present our experience in SLN detection and feasibility of sentinel using a single-dye technique (methylene blue).

Materials and Methods

This prospective study was conducted in a single surgical unit of a regional cancer center. The period of study was from January 2019 to December 2019. All patients with operable breast carcinoma, malignant melanoma of extremities, and penile carcinoma with clinically node-negative status were included after informed and written consent. All patients had normal renal function. Patients with palpable clinical nodes, those who received neoadjuvant chemotherapy, with recurrent tumor, T4 tumors, pregnancy, and prior surgery in the nodal basin were excluded. All patients underwent an ultrasound of the drainage nodal basin and if any radiologically suspicious node was detected, a guided fine-needle aspiration cytology was done to ensure clinical node negativity.

In patients with breast carcinoma, 5 mL methylene blue dye was taken and 2.5 mL each injected subdermally in the periareolar and the skin overlying the tumor. For penile cancer 5 mL was injected all around shaft of the penis subdermally. In patients with extremity malignant melanoma, 2.5 mL each was injected subdermally in the first web space and around the tumor area. Gentle massage was done for 2 to 3 minutes. The drainage basin was explored for sentinel nodes between 10 to 20 minutes after dye injection. The blue lymph node(s) were removed and sent for frozen section and for final histology. All patients underwent a formal lymph node dissection at the same sitting as completion of nodal basin surgery.

Results

The total number of nodal basins studied using the SNB procedure was 60. Primary tumor in 56.6% of patients was breast carcinoma, 40% penile carcinoma, and 3.4% was extremity malignant melanoma.

Sentinel node was successfully identified in 58 cases (96%). In two nodal basins, with carcinoma of penis, the sentinel node was not identified. Subsequent complete nodal dissection showed that the concerned nodal basins were pathologically negative. Out of the 58 cases, frozen section and final histopathology examination of the sentinel node were positive in 25.8% and negative in 70.6%. Frozen section result was positive and final histopathology report was negative in two cases (3.4%). The mean number of nodes identified in our study was 2.3 (►Tables 1 and 2).

Discussion

The first studies on the role of the lymphatic system in the spread of cancer cells and metastasis were performed in the 1950s.[11] Cabanas showed that the SLN was the first node to which a tumor drains in penile cancer. The observations provide evidence that tumor cells spread in an organized manner, following a predetermined anatomical pathway.[12] Giuliano was the first to propose the use of SLN biopsy in breast cancer patients using isosulfan blue injection into the tumor site.[6]

In the present study, SLN was identified in 96% of patients, which is similar to the result of the study done by Giuliano et al using isosulfan blue (96%).[6] SLN identification rate varies across studies, from 65 to 93% with blue dye, 91 to 98% with radiocolloid, and 90 to 97% with a combined method.[6,13-15]

Table 1 Patient characteristics

Primary tumor	No. of cases (n = 60)
Breast	34 (56.6%)
T1	8
T2	26
Penis	24 (40%)
T1a	8
T2	16
Melanoma	2 (3.3%)
T1	1
T2	1

Table 2 Histopathology characteristics

Tumor	True positive	True negative	False positive	False negative	Not identified
Ca Breast	12 (20.6%)	20 (34.4%)	2 (3.4%)	0	0
Ca Penis	2 (3.4%)	20 (34.4%)	0	0	2
Melanoma	1 (1.7%)	1 (1.7%)	0	0	0

Note: True positive: positive result in both frozen section and final histopathology. True negative: negative result in both frozen section and final histopathology. False positive: positive result in frozen section but final histopathology was negative. False negative: negative result in frozen section but final histopathology was positive. Not identified: node was not detected after dye injection.

In India, SLN detection using methylene blue dye injection has become a common practice due to its simplicity and cost-effectiveness. The use of radioactive isotope is not universal due to the constraints of cost and necessary apparatus. The unavailability of the latter should not be considered prohibitive to performance of a clinically important procedure like SLN biopsy because various studies have achieved comparable results between SLN using blue dye alone and SLN using a combined technique. Our study has explored the feasibility of performing the SLN procedure using the blue dye alone at our institute.

Study of SLN biopsy with methylene blue for staging the nodal basin was done with 100% sensitivity and 95.3% specificity. It was able to negatively predict the nodal basins in 100% patients, with an overall accuracy of staging being 96.5%, a false-positive rate of 4.6%, and 0% false-negative rate. For comparison, previous studies have variously reported identification rates between 71 and 93% and accuracy rates between 97 and 100% respectively using isosulfan blue as a single-dye technique.[6,16] However, if both techniques or only radioactive dye was used, the sentinel node detection rates and accuracy of the procedure ranged from 86 to 98% and 97.5 to 98%, respectively.[6,11-20] In previous reported studies, the sensitivity of the procedure of SNB was 88 to 89% when only blue dye was used compared with 92.2 to 94.2% when both techniques were utilized.[13,15]

Studies have reported hypersensitivity to isosulfan blue dye at rates of 1 to 2%.[16,19] In our study, none of the patients developed a hypersensitivity reaction to the methylene blue dye. In all these cases, a formal lymph node dissection followed the SLN biopsy procedure to test the accuracy of the latter. These results have given us confidence to perform the SLN biopsy procedure with blue dye alone without completing the formal lymph nodal dissection for node-negative basins.

Conclusion

SLN using a single-dye technique reliably identifies a sentinel node. This procedure can be safely adopted in patients with node-negative cancers as mentioned above to pathologically study the drainage basin.

Authors' Contribution

Concept: Gaurav Das, Joydeep Purkayastha, and Abhijit Talukdar.

Study design and methodology: Gaurav Das, Joydeep Purkayastha, and Abhijit Talukdar.

Data collection: Revanth Kodali, Sachin Khanna, Gaurav Das, and Lopamudra Kakoti.

Data analysis: Gaurav Das, Sachin Khanna, and Revanth Kodali.

Manuscript writing:Original draft—Revanth Kodali, Sachin Khanna, Gaurav Das, and Lopamudra Kakoti. Review—Gaurav Das, Joydeep Purkayastha, and Abhijit Talukdar.

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Conflict of Interest

None.

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