

CO-RELATION OF SENTINEL LYMPH NODE METASTASES WITH THE SIZE OF PRIMARY BREAST CARCINOMA

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ABSTRACT

This is a cross-sectional study designed to explore the co-relation between the tumour size and incidence of metastases in the sentinel lymph node and was conducted at Departments of Pathology, Punjab Medical College, Faisalabad and Sheikh Zayed Hospital, Lahore and Departments of Surgery, Allied & DHQ Hospitals, Faisalabad from July 2002 – June 2003. The sentinel lymph node (SLN) was identified in 80 cases of early (T1 & T2) breast carcinoma by a localization technique using 1% Isosulphan Blue. The maximum size of the tumour was measured on gross examination and the margins were labelled with Alcian blue and fixed in Bouin's fluid. The entire tumour was embedded and the size of the tumour was confirmed on microscopic examination. Similarly the entire SLN was embedded and the microscopic measurement of tumour deposit was made in every case. The SLN was successfully isolated in 80 cases. Right sided carcinoma was seen in 52.5%. Stage T1 was seen in 37.5% and 62.5% were of stage T2. Most of the tumours (65%) were located in the upper outer quadrant. Nearly all (97.5%) were infiltrating ductal carcinomas. The microscopic measurement of the size of tumour varied between 5-70mm and the size of the metastatic deposit of the tumour in the SLN varied from 2-22mm. It was noted that the involvement of SLN and non sentinel lymph node (NSLN) increased in relation to an increase in size of the primary tumour. The study concluded that as the size of the tumour increases, the chances of metastases occurring increases and thus has a linear relationship.

INTRODUCTUIN

Breast carcinoma is the most common malignancy affecting females. Its treatment is associated with considerable morbidity. A number of factors like tumour size, presence of in situ carcinoma, vascular invasion etc act as predictors of metastases in breast carcinoma¹. There is a strong correlation between tumour size and the incidence of axillary lymph node metastases. Early detection of breast carcinoma results in a declining number of patients with axillary lymph node metastases.² The sentinel lymph node (SLN) procedure is an accurate way to assess the axilla and avoid an axillary lymph node dissection in patients in whom the axilla does not contain metastases². The accurate staging of invasive breast carcinoma is a major objective in the management of this disease. For accurate staging tumour size and presence of metastatic disease in lymph node are indicators of outcome of patients with invasive breast carcinoma.

SLN procedure represents a sincere effort to reduce morbidity caused by axillary lymph node dissection, thus improving the quality of life for many breast cancer patients². This procedure has reduced the number of unnecessary lymphadenectomies. The information provided by the histology

of SLN together with the evaluation of the specific tumour phenotype and clinical features of each individual patient need to be considered for the provision of individualized treatment¹. We designed this study to evaluate the correlation between the size of tumour with the status of SLN metastases.

MATERIALS AND METHODS

The study was conducted in the department of Pathology Punjab Medical College, Faisalabad and Sheikh Zayed Hospital, Lahore and department of General Surgery Allied and DHQ Hospitals, Faisalabad from June 2002 to June 2003. Patients with unifocal breast carcinoma, diagnosed on FNAC or lumpectomy, where the primary tumour size was less than 5 cm (T1 & T2) without distant metastases and in whom SLN localization was successful were included in the study.

Before making the incision approximately 5 ml of 1% isosulphan blue was injected around the tumor or in the biopsy cavity if a lumpectomy had been done. The area was then massaged to improve the lymphatic uptake of the dye. Routine mastectomy with axillary clearance was performed in all cases. During the axillary dissection the blue stained lymphatic channels were followed to iden-

tify the SLN. This was isolated and excised. The axilla was then cleared.

The SLN was bivalved in the longitudinal axis and placed in formalin for fixation. The mastectomy specimen was placed in another container for fixation. Both the containers were labelled and sent for histopathology. Grossing was done after fixation according to the standard minimum dataset for reporting of breast cancer issued by the Royal College of Pathologists³. Serial sections of the mastectomy specimen were done and the tumour size was measured along its maximum dimensions. Then the maximum dimension was marked with Alcian blue and fixed in Bouin's fluid (Fig. 1). The entire tumour along the maximum length was then submitted for histopathology and the size on gross examination was confirmed microscopically. If previous lumpectomy had been done then the margins of the biopsy cavity were labelled with Alcian blue and fixed in Bouin's fluid. If the tumour was present microscopically in the margins of the biopsy cavity then the total size was estimated by adding the lumpectomy size with that of the margins of the biopsy cavity. If insitu component was present outside the main tumour it was added into the tumour to find out the final measurement of the tumour. The SLN was trimmed and all the fat was removed. The size was measured and the entire SLN was submitted for histopathology so as to avoid any false negative results.

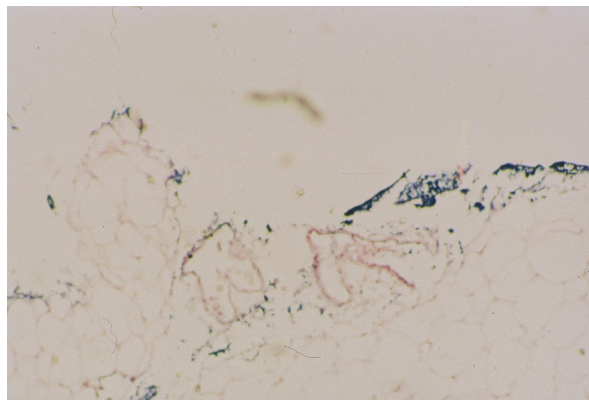


Fig. 1: Edge of tumour labeled with Alcian Blue.

The tissue was processed in Sakura tissue processor (Model RH-12E) embedded in wax, cut on the microtome and mounted on glass slides using the international criteria. These slides were then stained with H&E. If the SLN showed a reactive picture on histopathology, then levels were done till the entire tissue was finished and all levels were examined to detect metastases at any level (Figure 2). If the SLN showed tumour deposits then the tumour was measured in the maximum

direction. It was also seen whether there was any extranodal extension or not. The status of the NSLN was also evaluated. The results were tabulated and analysed using SPSS.

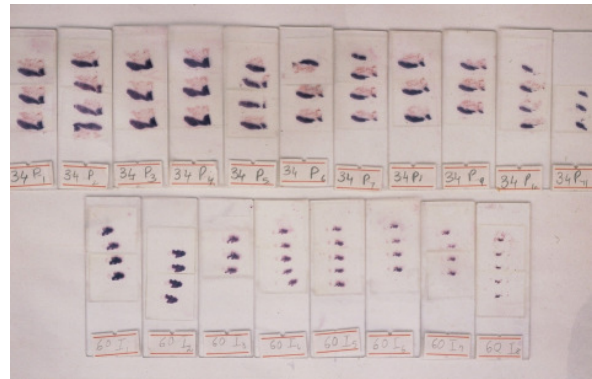


Fig. 2: Multiple levels done on Sentinel Lymph Node.

RESULTS

The dye was injected into 95 patients out of which SLN were identified in 80 cases which were included in the study. The mean age was 43.99+ 11.97 years ranging from 20 - 70 years. Forty two cases (52.5%) had right sided carcinoma. On clinical staging of the tumour 30 (37.5%) were of T1 stage and 50(62.5%) were of T2 stage. The dimensions of the lump were measured clinically (Table 1). The majority of tumours (65%) were found to be in the upper outer quadrant. Most of the tumours (97.5%) were of the infiltrating ductal variety and

Table 1: Dimension of the lump on clinical examination.

Size of the lump	Mean (SD)	Mode	Range
Length of lump	3.39 (± 1.10)	3	1 - 5
Breadth of lump	2.82 (± 1.01)	3	1 - 5

Table 2: Microscopic measurement of the tumour in millimetres.

Size of Tumour	Number
0 - 10 mm	3
11 - 20 mm	9
21 - 30 mm	20
31 - 40 mm	25
41 - 50 mm	11
51 - 60 mm	9
61 - 70 mm	3

91% were of grade II. The size of the tumour was evaluated microscopically (Table 2). The size of the tumour metastases in the SLN were measured and ranged from 2mm to 22 mm.

Table 3: Relationship between size of tumour and metastasis to the sentinel and non sentinel lymph nodes.

Size of Tumour	Mean	Median	Mode
SLN -ve (n=27)	26.704 mm	24 mm	22 mm
SLN +ve NSLN -ve (n=12)	32.833 mm	30.5 mm	30 mm
SLN +ve NSLN +ve (n=41)	39.195 mm	36 mm	33 mm

The relationship between the size of the primary tumour and the presence of the metastatic deposits in the SLN was explored. The cases were divided into three groups.

1. Cases with no metastases in the SLN and all the NSLN.
2. Cases with metastases in the SLN and reactive changes in the NSLN
3. Cases with metastases in the SLN and NSLN.

The tumour size in the groups was then compared. There were 27 cases in which the SLN showed reactive changes. Levels were done till the entire tissue was finished. These revealed no tumour deposit at any level and all the NSLN were also clear of the tumour. The mean size of the tumour in this group was 26.7mm. Out of the 53 cases in which the SLN revealed tumour deposit, it was seen that 12 had no tumour in the NSLN. The mean size of the tumour in this group was 32.8mm. Forty one cases of the total of 53 showed tumour deposit in the SLN and NSLN. The mean size of the tumour in this group was 39.2mm. (Table 3) Thus we demonstrated that the incidence of distant metastases increased directly in proportion with an increase in the size of the primary tumour. This relationship was also found to be statistically significant.

DISCUSSION

It is well known that the presence of lymph node metastases in breast carcinoma is directly proportional to tumour size¹. As with advances in diagnostic procedures currently majority of the newly diagnosed cases are increasingly node negative

and therapeutic decisions are based on the primary tumour characteristics. The most important of these is tumour size. Wilkinson⁴ in collaboration with the College of American Pathologists (CAP) issued guidelines for reporting. The CAP guidelines require measurements of gross tumour in three dimensions and the maximum tumour size as measured microscopically. The idea was not to omit the key elements that affect treatment. These include gross description, size, orientation, histologic features including Bloom Rishardson reporting of grade and the extent of in situ component.

The tumour size as determined by the pathologist from gross examination of the specimens can misinterpret actual tumour size dramatically both by underestimating the true extent of an invasive carcinoma and by over estimation of its size by inclusion of the contiguous areas of either proliferative breast lesion or post biopsy reactive changes.⁵ This is why in this study after labeling with Alcian blue and fixing in Bouin's fluid the actual size of the tumour was recon-firmed.

The study was designed to find out the relationship between tumour size and SLN metastases. It was seen that as the size of the tumour increased there was an increase in the axillary metastases which occurred in an orderly progression involving the SLN first. Then as the tumour progressed, this lead to the involvement of the NSLN. The same relationship was noticed by Tor-renga². He stated that an early detection of breast carcinoma resulted in a declining number of cases with axillary lymph node metastases¹. This implies that as the size of the tumour increases, the lymph node metastases occurs progressively. So the tumour size and the lymph node metastases are directly proportional to each other. There is a percentage of cases in which the metastases is limited to the SLN. It signifies that this lymph node is the first to harbour metastases and it can truly predict the axillary status. The importance of this is that if the patient presents early, the chances of metastases are less. In such cases SLN isolation can predict the axillary status and if the SLN is free of the disease then the axilla is also free of the disease.

Hwang et al⁶ conducted a study on 131 patients who had a positive SLN and underwent complete axillary clearance and it was seen that in 40- 60% of the patients in whom the SLN was the only positive lymph node the removal of the rest of the axillary lymph node was of no benefit to the patient. The risk of positive NSLN was 4.1times greater with primary tumour of size >2cm as compared to smaller tumour size. Dowlatsahi et al⁷ also studied the co-relation between the tumour size

and the SLN metastases in 200 patients with operable breast cancer and found a similar linear relationship between the tumour size and percentage of SLN metastases. Henry - Tillman et al⁸ conducted a study on 247 patients in whom SLN was identified by Tc labelled sulfur colloid, blue dye or both and found that the number of patients with T2 stage the positive SLN were more as compared to T1 stage.

Michaelson et al⁹ reported in his work in which size plus node method was used for integrating these two variables into an overall predictor of survival. They concluded that as the tumour size increases so does the proportion of lymph nodes positivity. Similarly Viale et al¹⁰ conducted a study on sentinel and non sentinel lymph nodes of 122⁸ patients and found out a similar relation ship.

As the tumour size and lymph node metastasis increases the mortality rate also increases. Michaelson et al thus concluded that prompt attendance at annual mammographic screening will reduce tumour size of breast carcinoma at the time of detection and hence will decrease the death rate in all age groups¹¹.

Primary tumour size and volume of disease in the SLN were significant indicators in the incidence of NSLN metastases in the regional basin. As the tumour size and the volume of SLN increases the incidence of NSLN metastases also increases¹². Rivers et al¹³ concluded in a study that patients with SLN micrometastases had very low incidence of nodal disease on complete axillary lymph node dissection. Patients with larger primary tumours, lymphovascular invasion and extranodal extension are more likely to have axillary lymph node disease that will affect the cancer management.

Thus, we **concluded** that the SLN is an accurate way to stage the axilla to avoid unnecessary lymph node dissection in patients in whom the axilla does not contain metastases and as the size of the primary tumour goes on increasing the chances of metastases in the SLN increase. So for decreasing the mortality rate earlier diagnosis and prompt treatment by SLN dissection must be carried out.

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