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Preservation of nipple-areola complex in breast cancer — a clinicopathological assessment☆

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Summary *Background:* Skin-sparing mastectomy (SSM) with immediate breast reconstruction (IBR), which traditionally includes the nipple-areola complex (NAC), is the modern way of improving the cosmetic and aesthetic outcome of advanced breast cancer surgery. However, with nipple and areola lacking, it fails to simulate the original breast. This study is directed at exploring the possibility of NAC preservation in selected mastectomy patients.
Methods: A retrospective analysis of the breast specimens of 219 consecutive mastectomy patients was performed after categorising the tumour characteristics on the basis of their TNM staging. The relationship of malignant involvement of the NAC with positive regional lymph nodes (pN), tumour size (T), site, stage and skin involvement by the breast tumour was noted and analysed. Chi-square analysis was performed for different characteristics vis-à-vis NAC involvement. Two-sided lists, wherever possible, had been performed at the 5% level of significance and *P* values were evaluated.
Results: The total frequency of malignant involvement of NAC was 44 (20%) out of 219. The frequency of NAC involvement in stage I and II tumours was found to be 9.38% compared to stage III tumours where it was 30%. The NAC was involved in 4 (2.5%) of 160 patients with peripheral tumours compared with 40 (68%) of 59 patients with tumours located centrally. Only 2 (1.5%) of 130 peripheral tumours bigger than 5 cm had malignant NAC involvement while the number in their central counterparts was much bigger (59%). Not a single breast cancer patient with skin involvement in the peripheral quadrants had any nipple-areola involvement.
Conclusions: NAC can be preserved in patients having stage I, II and III diseases with peripheral tumours less than 5 cm in size, irrespective of the nodal status and skin involvement.

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Female breast cancer is a major medical problem with significant public health and social ramifications.

The recent trend of performing skin-sparing mastectomy (SSM) with immediate breast reconstruction (IBR),[1–3] which includes artificial reconstruction of the nipple-areola complex (NAC) by skin grafting or tattooing, fails to simulate a normal one even after the best efforts of the surgeon to alleviate the sense of loss of a cosmetically significant organ.

Therefore, it appears that the preservation of the NAC can revolutionise the skin-sparing mastectomy technique by improving the cosmetic and aesthetic result of mastectomy with immediate breast reconstruction.

Material and methods

The present study was conducted after receiving proper approval from the Institutional Ethics Committee (IEC) of Medical College, Calcutta, which is a state-recognised body.

A total of 219 consecutive cases were collected for this retrospective analysis, who had been treated with mastectomy at various institutions in Calcutta between January 2003 and June 2005. The pathologic sectioning was done by bread-loaf sectioning (vertical) of the nipple at 2 mm intervals, the depth being 1 cm and by tangential sectioning of the areolar base. The sections were then stained using H&E stain & viewed under a high power field (HPF).

These cases were then categorised on the basis of their TNM Staging.[4]

Each of the 219 cases, after categorisation, had been studied in detail under the following headings: tumour size (T), positive regional lymph nodes (pN), site of tumour, stage of tumour, malignant involvement of the NAC and skin involvement by the breast cancer. The location of the tumours was classified into central and peripheral, central being those which were subareolar within 2 cm from the outer margin of the areola, while peripheral tumours were those which were located in the upper outer, upper inner, lower outer and lower inner quadrants, not encroaching within 2 cm from the areolar margin.

Chi-square analysis was performed for different characteristics vis-à-vis NAC involvement. Location of tumour being considered as one of the most important factors, combination of effect with this parameter had been studied for each of the other tumour characteristics. Two- sided lists, wherever possible, had been performed at the 5% level of significance and *P* values were evaluated.

Results

The total frequency of malignant involvement of the NAC was 44 (20%) of 219 (Table 1). Of these, the incidence of isolated areola involvement was only two (0.9%). Eight (37%) of 22 patients with central tumours in stage I/II disease while 32 (86%) of 37 patients, with central tumours in stage III disease, presented with malignant involvement of the NAC.

When comparing patients with tumours ≤ 5 cm with patients with tumours > 5 cm, NAC involvement occurred in 15% and 38%, respectively ($P = 0.04$). In T ≤ 5 cm, only 2 (1.5%) of 130 peripheral tumours had malignant NAC involvement. The tumour sizes varied from 1.2 cm to 14 cm with skin involvement concomitant with NAC involvement in 24 cases.

Table 1 Tumour characteristics with respect to malignant NAC involvement

Tumour characteristics	Patients with NAC involvement	Total number of patients, $n = 219$
<2 cm	1(7.14%)	14
2 to 5 cm	24(15%)	155
>5 cm	19(38%)	50
Node negative	11(15%)	74
<4 nodes	10(21%)	48
4 to 9 nodes	14(22%)	65
≥ 10 nodes	9(35%)	26
not known	—	6
Stage I	1(17%)	6
Stage II	8(8.99%)	89
Stage III	35(30%)	118
not known	—	6

The frequency of malignant NAC involvement was highest in the ≥ 10 nodes category (35%) ($P < 0.001$). However, even in this classification, central tumours had an overall predominance over the peripheral tumours with respect to malignant infiltration of the NAC.

When categorised by the stage of tumour, the frequency of NAC involvement in stage I and II tumours was found to be 9.38% compared to stage III tumours where it was 30%. Only 1 of 73 (1.37%) peripheral tumours had malignant NAC involvement in stages I and II ($P < 0.001$).

Location of the breast cancer was the only criterion that reliably predicted nipple-areola involvement. The NAC was involved in only 4 (2.5%) of 160 patients with tumours located in the lower inner, lower outer, upper inner or upper outer quadrants of the breast, compared with a huge 40 (68%) of 59 patients with tumours located in central or retro-areolar areas of the breast (Table 2) ($P < 0.001$).

Out of the 47 patients who presented with T4 lesions, i.e. with skin involvement of the cancer, 24 patients showed malignant involvement of the NAC. Twenty-four out of 24 patients who had a centrally located tumour with skin involvement showed malignant infiltration of the NAC (Table 3) ($P < 0.001$). However, there were two cases where the fungating mass encroached into the areola from the adjacent area and involved it without affecting the nipple. None of the 23 patients, having peripherally-located tumours with skin infiltration, had any NAC involvement.

Discussion

The malignant involvement of the NAC in this retrospective study comprising 219 consecutive cases was 20%. Several studies in the past had shown malignant involvement of the areola/nipple to be present in 5.6 to 45.5% of mastectomy specimens.[5–12]

In the present study, one factor had emerged very strongly which governed malignant NAC infiltration, i.e. the site of the tumour. It was observed that advanced