Association of Histomorphological Prognostic Factors of Invasive Breast Carcinoma - NST with Axillary Lymph Node

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ABSTRACT

Background: Breast carcinoma is one of the leading malignancy in women. Surgical MRM specimen histology and prognostic factors play important role in management of the patient and need to be examined in detail to help clinician for better treatment options.

Materials and methods: Two-year study of MRM specimens which were IBC-NST were included. Gross and microscopic prognostic factors were studied and analysed with axillary lymph node involvement, using Bivariate analysis by Chi Square using SPSS.

Results: Total 141 cases were studied. Maximum (59%) cases had tumor size between 2.1-5cm. According to modified RB tumor grading system, 48% had Grade-III and 44% had Grade-II tumor. Tumor emboli were positive in 60.7% and tumor necrosis was positive in 47% cases. Retracted nipple was seen in 38% of cases. Both ER/PR were found positive in 43%cases and both ER/PR were found negative in 52% cases, HER2 was negative in 72%cases. Axillary lymph nodes were not involved in 45.4% cases, while 19.1%, 14.9% and 10.6% cases were positive for 1-3, 4-7 and 8-10 axillary lymph node involvement respectively. Statistically significant association (p< 0.05) of axillary lymph node was found with Tumor emboli, HER2 status, ER/PR status, Tumor size, Nipple Areola Complex and Overlying Skin. Borderline association (p nearing 0.05) was found with Skin involvement by tumor and Tumor grade.

Conclusion: Axillary lymph node status is an important prognostic factor in breast carcinoma and it is found associated with other important histomorphological prognostic factors which needs to be evaluated thoroughly for better post-operative patient care.

Keywords: Breast carcinoma, Axillary lymph node, histomorphological prognostic factors,

INTRODUCTION

All over the World breast carcinoma is one of the most frequent cancers in women and is the second leading cause of cancer death in women.[1,2]A number of pathological characteristics have been identified, which can be used as prognostic factors, including tumor size and grade, ER/PR receptor, HER2, and lymph node status[3] which are all considered when predicting prognosis and determining the most effective treatment options.

Axillary lymph node metastasis is one of the most important prognostic parameters.[4]The most common site of lymph node involvement is axilla, followed by supraclavicular and internal mammary nodes. Not only is there a sharp difference in survival rates between patients with positive and negative nodes, but the survival

rate also depends on the level of axillary node involved (low, medium, or high), the absolute number (fewer than four versus four or more)[5]. For prognostic purposes, the best grouping seems to be the following: negative nodes, one to three positive nodes, and four or more positive nodes. Increasing histologic grade is also associated with higher incidence of positive axillary nodes. Patients with positive axillary nodes have higher loco-regional recurrence rate than those with negative axillary nodes and the rate of recurrence increases with the number of positive nodes.

Sentinel lymph node: First pioneered in the first half of the 1990s, the technique of sentinel lymph node biopsy for the evaluation and management of breast carcinoma has gained enormous popularity, and is regarded by many as becoming or having become the standard of care.[6] The procedure is based on the concept that if the sentinel node is negative, the other nodes of that group will also be negative in nearly all instances, whereas if it is positive, the chance that there will be additional metastases in that nodal group is about one-third.

MATERIALS & METHODS
The study was carried out in department of Pathology, at a tertiary care hospital and two-year data of MRM specimen was taken.

Inclusion Criteria was: All MRM specimens with axillary node dissection diagnosed to be invasive breast carcinoma-no special type on microscopy were included.

Exclusion Criteria was: All cancer cases diagnosed other than Invasive breast carcinoma-NST.
Ethics Clearance from institute and Informed Consent from patient were taken. Gross findings of specimen were recorded from the pathology report in the files. Histology sections of specimen were retrieved and reviewed to confirm the

findings of histopathology. Tumor grading was done according to modified Bloom Richardson by Elston and Ellis method. Gross prognostic factors like Tumor size, gross necrosis, haemorrhage, surgical margins number of lymph nodes in axillary tail were noted. In microscopic prognostic factors like Tumor necrosis, tumor emboli, tumor grade, host immune reaction, number of positive lymph nodes were noted. Immuno-histochemistry prognostic factors: ER, PR and HER2 hormone receptors were done and reported as per standard protocol.

STATISTICAL ANALYSIS
To find correlation of all histomorphological prognostic factors with axillary lymph node status, Bivariate analysis by Chi Square was done for all gross and microscopic histomorphological prognostic factors separately by using SPSS software.
After analysis, all the demographic and histomorphological factors were then grouped into following four categories (wherever possible): -

A. Factors not associated
B. Borderline statistically significant factors (P nearing 0.05 but > 0.05)
C. Statistically significant factors (P< 0.05)

RESULT
In two years, 141 cases were reported as IBC-NST and were included for analysis.
Maximum number of patients(1/3rd) were from 5th decade. According to site, left sided carcinoma was seen in 60% of the cases and nearly 42% of cases, tumor was present in upper outer quadrant. In 2/3[rd]of the patients lump was not fixed to underlying tissue.
Nearly 59% cases had tumor size between 2.1-5cm and 29% had tumor of size between 5.1-10cm. According to modified RB tumor grading system, 48% had Grade-III and 44% had Grade-II tumor. Tumor emboli were positive in 60.7% and tumor necrosis was positive in 47% cases. Nipple areola complex was found normal in 60% of cases and retracted nipple was seen in 38% of

cases. Both ER/PR were found positive in 43% cases and both ER/PR were found negative in 52% cases, HER2 was negative in 72% cases and positive in 28% cases.

Axillary lymph node: Axillary lymph nodes were not involved in 64 (45.4%) cases, while 27(19.1%), 21 (14.9%) and 15 (10.6%) cases were positive for 1-3, 4-7 and 8-10 axillary lymph node involvement respectively. 14 cases (9.9%) were positive for more than 10 axillary lymph node involvement.

No. of lymph nodes involved	Frequency	Percent
0	64	45.4
1-3	27	19.1
4-7	21	14.9
8-10	15	10.6
>10	14	9.9
Total	141	100

Table:1 Number of axillary lymph node involved

All 141 cases were analyzed for evaluation of association of "Axillary lymph node involvement" with following demographic and histomorphologic factors as: age, parity, site of lump, location of lump, duration of lump, consistency, tumor fixation to underlying tissue, overlying skin change, nipple areolar complex change, multicentricity, tumor size, tumor grade, tumor emboli, tumor necrosis, skin involvement by tumor cells (on microscopy), ER/PR status and HER2 status.

A. No association of axillary lymph node involvement was found with:

Age, Parity, Site (Left or Right), Fixity to tissues, Multicentricity, Tumor necrosis, Lump location, Duration of lump, Consistency

B. Borderline statistically significant association of axillary lymph node involvement was found with:

1. Skin involvement by tumor cells (ALN involvement was found in 53% cases if skin was not involved as compared to 85.7% cases when skin was involved)
2. Tumor grade (ALN involvement was found in 36.4% cases in grade-I as compared to 62.9% and 50% cases with grade-II and grade-III respectively)

Parameter name	Specifics of parameter	Axillary LN involvement (%)	P-value
Skin involvement by tumor cells	Yes	85.7%	0.064
	No	53%	
Tumor grade	I	36.4%	0.083
	II	62.9%	
	III	50%	

Table:2 Association between axillary lymph node involvement and prognostic factors, with P value

C. Statistically significant association of axillary lymph node involvement was seen with:

1. **Tumor emboli** (ALN involvement was found in 32.2% cases if tumor emboli were absent as compared to 65.1% cases when tumor emboli were present)
2. **HER2 status** (ALN involvement was found in 51% cases when HER2 was negative as compared to 64.1% cases when HER2 was positive)
3. **ER/PR status** (ALN involvement was found in 49.2% cases when both ER/PR were positive, 56.2% cases when both ER/PR were negative and 85.7% cases when either one of ER/PR was negative)
4. **Tumor size** (ALN involvement was found in 38.5% cases with tumor size up to 2 cm, 47% when tumor size was 2.1-5 cm and 73.3% cases when tumor size was >5 cm)
5. **Nipple Areola Complex** (ALN involvement was found in 42.4% cases when nipple areola was normal as compared to 71.2% cases when nipple areola was abnormal)
6. **Overlying Skin** (ALN involvement was found in 45.7% cases when overlying skin was normal as compared to 71.4% cases when overlying skin was abnormal)

Parameter name	Specifics of parameter	Axillary LN involvement, (%)	P-value
Tumor emboli	No	32.2%	0.010
	Yes	65.1%	
HER2	Positive	64.1%	0.011
	Negative	51%	
ER/PR	P/P	49.2%	0.025
	N/N	56.2%	
	Other (P/N, N/P)	85.7%	
Tumor size	Up to 2 cm	38.5%	0.005
	2.1-5 cm	47%	
	>5 cm	73.3%	
Nipple areola complex	Normal	42.4%	0.002
	Abnormal	71.2%	
Overlying Skin	Normal	45.7%	0.005
	Abnormal	71.4%	

Table:3 Statistically significant factors association with axillary lymph node involvement

DISCUSSION

Study by Cserni et al[7] concluded that some researchers consider only the lymph node status as most important significant prognostic factor for survival and for disease free period of illness. In present study 45.4% patients were negative for axillary lymph node involvement, whereas 19.1%, 14.9%, 10.6% and 9.9% were positive for 1-3, 4-7, 8-10 and >10 axillary lymph node involvement respectively.

Statistically significant association (P<0.05) of axillary lymph node involvement was found with tumor emboli, HER2, ER/PR status, tumor size, abnormal nipple areola and abnormal skin, whereas border line statistically significant association for finding positive axillary lymph nodes was found with tumor grade and skin involvement with tumor cells.

Tumor size and axillary lymph nodes

Present study found 38.5%, 47% and 73.3% cases positive for axillary lymph nodes with tumor size up to 2 cm, 2.1-5 cm and > 5.1 cm respectively. Patrana et al[8] found an association between increasing tumor size with increase percentage of lymph node metastasis with in turn leads to worse prognosis, some other studies also mention the same.[9]

Tumor grade and axillary lymph nodes

In present study we found 36.4%, 62.9% and 50% cases positive for lymph nodes with grade-I, grade-II and grade-III tumors respectively. High grade tumors are associated with more incidence of axillary lymph node metastasis. According to Hopton DS high grade tumors are associated with increased incidence of axillary node metastasis with four or more nodes as compared with low grade tumors.[10] Many other studies also concluded the same.[11,12]

Tumor emboli and axillary lymph nodes

This study showed that when tumor emboli were absent, incidence of positive lymph nodes were 38.2% as compared with 65.1% incidence of positive lymph nodes when tumor emboli were present.

ER/PR, HER2 and axillary lymph nodes

present study showed 64% of patients with positive HER2 were found axillary lymph node involvement. One study found that node-positive patients who were HER2+ had a lower 10-year overall survival proportion, 50% versus 65% for those who were HER2-.[9]

Nipple areola complex with overlying skin and axillary lymph node

In present study 38% presented with retracted nipple and 1.4% presented with ulcerated or eroded nipple areolar complex. Similarly, 35% presented with dimpling/ peau-d-orange/ulceration or discoloration of skin.

Both abnormal skin and abnormal nipple areola complex occurs late and suggests long standing and advanced local disease which causes metastasis to axillary lymph nodes.

Ignorance, painless symptoms, poor socio-economic status, lack of medical resources, social barrier can be attributed to late presentation.

CONCLUSION

This study showed that women operated in our tertiary care hospital, presented with advance stages of breast carcinoma. Axillary lymph node metastasis is an important prognostic factor in determining the prognosis and it was found positive in more than half of the patients. Positive axillary lymph nodes are further significantly associated with tumor emboli, HER2, ER/PR status, tumor size, abnormal nipple areola and abnormal skin. Therefore, these histomorphological factors has to be carefully evaluated in patients who have positive axillary lymph nodes in MRM specimens for better treatment and prognosis.

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