Histomorphological Analysis of Invasive Breast Carcinoma in a Tertiary Care Center

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Abstract
Background: Breast carcinoma is the most common malignant tumor and also one of the leading cause of the carcinoma deaths in women. There are many prognostic factors established for breast carcinoma. The most important prognostic factors of breast cancer are tumor size, histological grade and lymph nodal stage.

Objectives: To study the relative frequency, distribution and histomorphological features of breast carcinoma in the study group.

Materials and Methods: A total of 165 breast carcinoma specimens (Mastectomy) were enrolled between the period of September 2014 to August 2016. Age, tumor size, tumor grade, necrosis, associated breast lesions, lymph node involvement, lymphovascular invasion, lymphocytic response, skin infiltration, margin status were analyzed.

Results: Median age of the study group was 49 years. Invasive Carcinoma - Not Otherwise Specified was the commonest type, 38 cases (23%) had tumor less than 2 cm, 99 cases (60%) were of 2 to 5 cm in size and 28 cases (17 %) were more than 5 cm in size, 56.4% were grade 2 tumors. Node positive cases were 58.25 % (n=96), Skin infiltration was seen in 6.1% (n= 10), necrosis was seen in 47.3% (n=78), Lymphovascular invasion was seen in 74.5% (n=123), Positive margins were noted in 7.9% (n=13). Lymphocytic infiltration response was seen in 74.5% (n= 123).

Conclusion: Invasive carcinoma was the most common type. Incidence was more common at younger age group as compared to western population. More than half of the patients presented with lesser tumor size, lymph nodal metastasis, lesser grade and more lymphocytic response. This study population had better prognostic factors.

Introduction
Breast carcinoma is the most common malignant disease and the leading cause of cancer deaths in females with more than 1 million cases being reported globally annually.[1] In United States, around 1 lakh new cases are diagnosed annually and around thirty thousand women die due to breast carcinoma. In India, the crude incidence
rate of breast carcinoma is 85 per one lakh women per year[2]
Breast cancer is more common in 50-60 years of age constituting 69% of breast cancer. India is rapidly moving towards industrialization which results in lifestyle changes. This is probably the reason for increase in breast cancer incidence in India. The most important prognostic factors of breast cancer are tumor size, histological grade and lymph nodal stage.

The evaluation of the prognostic factors to provide the prophecy of outcome has become an important role of the histopathologist in handling and reporting the invasive breast carcinomas. We aimed to identify the relative frequency and distribution of breast carcinoma and to study the histomorphological features of breast carcinoma including histological subtypes, grade, lymph node status, lymphovascular invasion, lymphocytic response, necrosis and skin infiltration in our study population.

Materials and Methods
This study is a descriptive prospective and retrospective study of Primary breast carcinomas conducted in the Institute of Pathology, Madras Medical College and Rajiv Gandhi Government General hospital, Chennai during the period between September 2014 to August 2016. The study includes all modified radical mastectomy specimens of breast carcinomas. All small biopsies and recurrent tumors were excluded from the study.

Detailed history of the cases regarding age, sex, side of the breast, type of procedure, details of gross characteristics such as tumor size, nodal status were obtained for those 165 cases from surgical pathology records. Formalin fixed tissue were cut, processed and paraffin embedded. Four μm thick sections of the paraffin tissue blocks were cut and stained with eosin and hematoxylin. Slides were collected from slide filing and were reviewed and graded using the Nottingham modification of the Scarff Bloom Richardson Grading system and they were further evaluated for the presence of necrosis, lymphocytic response, lymphovascular invasion and skin infiltration. Staging of tumor and nodal involvement was done using TNM staging system, AJCC, ed. 8.

Results
The total number of breast carcinomas enrolled in this study period was 165 cases. The highest incidence of breast cancers was found in the age group of 41-50 years. The median age of the patient in this study was 49. The youngest age of presentation of breast cancer was 30 years in this study. 77 cases of primary breast carcinomas were reported in left breast and 88 cases were reported in right breast. 66 cases of breast carcinoma were in upper outer quadrant. Thirty eight cases (23%) had tumor less than 2 cm, 99 cases (60%) were of 2 to 5 cm in size and 28 cases (17 %) were more than 5 cm in size. Commonest histopathological subtype in this study was IDC NOS which constituted 93.9% (n=155) of cases and other subtypes were metaplastic carcinoma (n=3), mucinous carcinoma (n=5), apocrine carcinoma (n=1) and intracystic papillary carcinoma (n=1).

Tumor grade was done according to modified SBR grading system, low grade (grade 1 and 2) includes 83.7% (n=138) and high grade (grade 3) seen in 12.1%(n=20) only. 62 cases (37.6%) had upto 3 nodes with metastatic carcinomatous deposits, 25 cases (15.2%) had 4 to 9 involved nodes, 9 cases (5.5%) had more than 10 involved nodes, while 69 cases (41.8%) had no nodal involvement.

Positive margins were noted in 7.9% (n=13) and adequate margins were noted in 92.1%(n=152) cases. Lymphovascular invasion seen in 74.5% (n=123) and absent in 25.5% (n=42) cases. Lymphocytic infiltration was seen in 123 cases (74.5%). 78 out of 165 cases (47.3%) had necrosis. Skin infiltration was seen in 10 out of 165 cases, which constituted 6.1%. 
| CHARACTER | n (%) | CHARACTER | n (%) |
|---------|-------|---------|-------|
| **SIDE** |       | **TYPES** |       |
| RIGHT   | 88(53.3%) | INVASIVE CA NOS | 155(93.9%) |
| LEFT    | 77(46.7%) | METAPLASTIC CA | 3(1.8%) |
| QUADRANT |       | IDC WITH MUCINOUS CA | 5(3.0%) |
| UOQ     | 66(40%)  | APOCRINE CA | 1(0.6%) |
| UIQ     | 25(15.2%) | INTRACYSTIC PAPILLARY CA | 1(0.6%) |
| LOQ     | 22(13.3%) | MARGINS |       |
| LIQ     | 17(10.3%) | PRESENT | 13(7.9%) |
| CENTRAL | 35(21.2%) | ABSENT | 152(92.1%) |
| **SIZE** |       | **LYMPHOVASCULAR INVASION** |       |
| T1      | 38(23.0%) | PRESENT | 95(57.6%) |
| T2      | 99(60%)  | ABSENT | 70(42.4%) |
| T3      | 28(17%)  |       |       |
| **NODAL** |     | **SKIN INFITRATION** |       |
| N0      | 69(41.8%) | ABSENT | 42(25.5%) |
| N1      | 62(37.6%) |       |       |
| N2      | 25(15.2%) | PRESENT | 10(6.1%) |
| N3      | 9(5.5%)  | ABSENT | 155(93.9%) |
| **GRADE** |   | **ASSOCIATED LESION** |       |
| UNKNOWN | 7(4.2%)  | PRESENT | 78(47.3%) |
| GRADE I | 45(27.3%) | ABSENT | 87(52.7%) |
| GRADE II | 93(56.4%) | NIL |       |
| GRADE III | 20(12.1%) | FIBROCYSTIC DISEASE | 95(57.6%) |
|         |         | DUCTAL CARCINOMA INSITU | 30(18.2%) |
|         |         | ADENOSIS | 5(3.0%) |
|         |         | ATYPICAL DUCTAL HYPERPLASIA | 3(1.8%) |
|         |         | EPITHELIAL HYPERPLSIA | 2(1.2%) |
|         |         | FIBROADENOMA | 6(3.6%) |

**Distribution of Histological Type**

| HISTOPATHOLOGY | NO OF CASES(n) |
|----------------|----------------|
| IDC NOS        | 155            |
| Metaplastic CA | 3              |
| Mucinous CA    | 5              |
| Apocrine CA    | 1              |
| Intracytic Papillary CA | 1 |

**Distribution of Size of the Tumor**

| TUMOUR SIZE(in cms) | NO OF CASES(n) |
|---------------------|----------------|
| <2                  | 38             |
| >02 ≤ 05            | 99             |
| >5                  | 28             |
Distribution of Histological Grade

Distribution of Lymph Node Metastasis in Breast Cancers

Distribution of Lympho Vascular Invasion in Breast Cancer

Ductal Carcinoma of Breast

Figure 6. Infiltrative grey white, firm growth with irregular margins

IDC Grade 1

Figure 7. Malignant duct epithelial cells arranged in tubules with mild nuclear pleomorphism (400x)

IDC Grade 2

Figure 8. Malignant duct epithelial cells in tubules and sheets with moderate nuclear pleomorphism (100X)
Figure 9. Malignant duct epithelial cells in sheets with marked nuclear pleomorphism and increased mitosis (400x)

Mucinous Carcinoma

Figure 10. Well circumscribed glistening gelatinous growth

Figure 11. Tumor nests floating in pools of mucin(400x)

Intra cystic papillary carcinoma

Figure 17 Microscopy -100x

Lymphovascular Invasion

Figure 19 Microscopy 400X.

Discussion
Breast cancer is the most common cancer in the urban women and second common cancer in rural women. It is a heterogeneous disease with varying clinical and pathological presentation. We can reduce the mortality of breast cancer by early detection, appropriate management and targeted therapies. Many theories underlie the pathogenesis of breast cancer and there are many prognostic factors including histological subtypes, grade, lymph node status, lymphovascular invasion, lymphocytic response, necrosis and skin infiltration.

Madras Medical College being a tertiary care center, among the surgical specimens received, breast specimens include 6.33 % of all cases. Malignant breast tumors constituted 40.5% of all the breast specimens received.

The youngest age presented with invasive ductal carcinoma was 30 years and oldest age reported was 75 years with 49 as median age of
presentation. This compared with study by Micello et al,[3] Carreno et al,[4] Hu et al,[5] Honma et al[6] showed that in India there is a change in trend towards younger age group in the recent years. Breast cancer seems to be more common in the younger age group in India and 52% of all women suffering from breast cancer in Mumbai are between 40 and 49 years of age[7-11]. The highest incidence of breast cancer was reported in 41 to 50 years age group. This is in concurrence with the study done by RajeshSingh Laishram et al.[12]

Among the histological types, Invasive ductal carcinoma NOS type comprised the most common with 93.3%. This correlated with the study done by Albrektsen et al,[13] Shirley SE et al[14] and AM Dauda et al. [15] The incidence of IDC NOS type is higher in Indian women (89.62%) compared to that of western women accounting for the poor prognosis. According to Shet T et al study, the incidence of mucinous carcinoma is 2% to 3% and also intracystic papillary carcinoma commonly seen in our Indian population which is comparable to our study.[16]

Majority of the breast carcinomas were T2 stage which is similar to the study done by Lakmini et al[17]. But comparing with the study by Christine L[18] and Carter et al the proportion of T2 in Indian population (70.28%) is higher than in Western population (55.4%).

The Grade II tumors were more common than other grades of breast cancers. This observation coincides with the study done by QiJ et al[19]. Careyet al[20] and G GVanden Eynden et al[21].

Fifty eight percent of the cases showed lymph node metastasis and 37.6% cases with 1-3 nodes positive. These data coincide with the study done by Jun Quet al[13] and S E Shirley et al[9] who reported nodal metastasis in 60.32% and 75.7% of their cases.

In our study there was lymphocytic infiltration in 74.5%, skin infiltration in 6.10% and necrosis in 47.3% of the cases, but there was 33% skin infiltration reported in the study conducted by Chanda Bewtra et al[16] and 38.1% necrosis in the study conducted by Gloria Perio et al[17].

Conclusion

Invasive carcinoma is the most common type. Incidence is more common at younger age group as compared to western population. More than half of the patients presented with lesser tumor size, lymph nodal metastasis, lesser grade and more lymphocytic response. This study population had better prognostic factors.

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