Histopathological Prognostic Factors In Carcinoma Breast - An Indian Institutional Experience

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Abstract

Objective: Pathological prognostic factors in breast cancer are now widely used to predict biological behavior of cancer and to plan its effective management. In this paper, we attempt to evaluate the reports from our histopathology laboratory spanning over a period of 2 years. The aim of this descriptive study was to see the various histopathological features of breast cancer in order to know the pattern of disease in recent time in India. **Methods:** The pathology reports of primary carcinoma of the breast diagnosed in our laboratory from 1st January 2010 to 31st December 2012 (2 year period) were reviewed for details on tumor size, histological type and grade, presence or absence of tumor emboli in vascular channels and lymph node status. **Results:** Total of 174 patients was included in the study. The mean age of presentation was 47.84 years. In 86 cases the lump was palpable in the upper lateral quadrant, followed by 52 cases in the upper medial quadrant. Duct cell carcinoma was the most common histological subtype (148 cases) accounting for 85% of the cases. Mucinous carcinoma was the second most common, occurring in 7 cases (4%). 81.61 % of tumours were grade II. Highest number of tumours were detected in the T2 stage i.e with size varying between 2 – 5 cms (67.24%). In decreasing frequency T3 > T1 > T4 stage tumours were observed. More number of cases in our study population belonged to either N0 category or N1 category. 90 cases had lymphovascular invasion in our study accounting for 51.72%. **Conclusion:** Our study puts forth the trends in histopathological prognostic factors in primary carcinoma breast in India.

Keywords: Carcinoma Breast, Prognostic Factors, Tumor Size, Histological Type, Grading, Lymph Node Status.

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Introduction

Carcinoma of the breast is the commonest malignancy of females all over the world and second leading cause of death due to cancer among females [1]. It can occur at any age but is rare in patients younger than 25 years and over 80 years; the peak incidence is 45 to 50 years in Indian population [2]. Although invasive carcinoma of the breast was clinically regarded as a single entity in the past, histologic and molecular analysis have demonstrated that breast cancer is a heterogeneous disease, composed of morphologically and genetically distinct entities with different molecular profiles, behavior, and response to therapy. Clinically, invasive breast cancer is classified according to primary tumor size, lymph node status, and local extent and presence of distant spread. At the morphologic level, breast cancer is classified according to histologic types and grades [3].

A considerable amount of important prognostic

information is available from the careful histopathologic examination of breast carcinoma specimens. The college of American Pathologists ranks prognostic and predictive factors into three categories: category I, factors proven to be of prognostic import and useful in clinical patient management; category II, factors that had been extensively studied biologically and clinically, but whose import remains to be validated in statistically robust studies; and category III, all other factors not sufficiently studied to demonstrate their prognostic value [4]. With a wide range of therapeutic modalities available, focus has been laid to treat the disease on an individual basis.

Factors ranked in category I included TNM staging information, histologic grade, histologic type, mitotic figure counts, and hormone receptor status. Category II factors included c-erbB-2 (Her2-neu), proliferation markers, lymphatic and vascular channel invasion, and p53. Factors in category III included DNA ploidy analysis, microvessel density, EGFR, TGF-α, bcl-2, pS2, and cathepsin D[4]. In our single institutional study we

endeavoured to analyze TNM stage, histological type and grade, lymphatic and vascular invasion in breast carcinoma in a subset of Indian population.

Materials and Methods

This is a two year retrospective study that takes into account breast cancer relevant data retrieved from the archives of department of Pathology, Indian Red Cross Hospital, Nellore, Andhra Pradesh, India. All cases that underwent modified radical mastectomy (MRM) following a trucut biopsy confirmation of breast malignancy between 2010 and 2012 were included. Patient's age, clinical details were obtained from the case files. Histopathological data that was documented after microscopic analysis of Hematoxylin and Eosin stained slides following routine formalin fixation and processing was also retrieved and studied. Grading and staging were done according to the Nottingham modification of the Bloom and Richardson grading system and TNM staging

respectively [5]. Cases were scored according to the Nottingham Prognostic Index (NPI)[6].

Nottingham modified system [5] is as follows:

Tubule Formation
Majority of tumor (>75%) 1 point
Moderate degree (10%-75%) 2 points
Little or none (<10%) 3 points

Nuclear Pleomorphism
Small, regular uniform cells 1 point
Moderate increase in size and variability 2 points
Marked variation 3 points

Mitotic Counts
Dependent on microscope field area* 1-3 points

Individual scores when added provide the grade of the tumour.

Results

There were a total of 174 MRM cases during the period of study. The youngest age at presentation was 28 years while the oldest being 75 years. The mean age of presentation was 47.84 years.

In 86 cases the lump was palpable in the upper lateral quadrant, followed by 52 cases in the upper medial quadrant. In 31 cases the lump was retroareolar. 3 cases had presentation in the lower lateral quadrant and 2 cases had the lesion in lower medial quadrant.
The incidence patterns of histological variants are put forth in Table 1.

Table 1: Incidence of various histological types of breast carcinoma in the current study

Histological Type	No. of Cases in Current Study (%)
Duct cell carcinoma, NOS	148 (85.05 %)
Mucinous	7 (4.02 %)
Medullary	4 (2.3 %)
Lobular	4 (2.3 %)
Squamous	3 (1.72 %)
Papillary	3 (1.72 %)
Signet ring	2 (1.15 %)
Apocrine	1 (1.15 %)
Cribriform	1 (1.15 %)

Duct cell carcinoma was the most common histological subtype (148 cases) accounting for 85% of the cases. Mucinous carcinoma was the second most common, occurring in 7 cases (4%). One case was diagnosed with intraductal carcinoma. 8 cases of duct cell carcinoma had associated Paget's disease of the nipple

Table 2: Classification based on the modified Scarff Bloom Richardson grading system

Degree of differentiation	Nottingham Grade (Score)	Number of cases (%)
Well Differentiated	I (3 – 5)	15 (8.62%)
Moderately Differentiated	II (6 – 7)	142 (81.61%)
Poorly Differentiated	III (8 – 9)	17 (9.77%)

Table 3: Distribution based on tumour size and axillary lymph nodal status

Tumour Size (T stage)	Number of cases (%)	Axillary Lymph nodes (N stage)	Number of cases (%)
T1 (≤ 2 cms)	21 (12.07 %)	N0 (No nodes)	68
T2 (> 2 cms - < 5 cms)	117 (67.24 %)	N1 (1 – 3 nodes)	56
T3 (≥ 5 cms)	22 (12.64 %)	N2 (4 – 9 nodes)	38
T4 (Any size with chest wall or skin extension)	14 (8.46 %)	N3 (≥ 10 nodes)	12

In our study we found that 90 patients had lympho-vascular invasion and 7 patients had perineural invasion.

Discussion

With rising incidence and awareness, breast cancer is the commonest cancer in urban Indian females, and the second commonest in the rural Indian women [7]. Over 100,000 new breast cancer patients are estimated to be diagnosed annually in India [8, 9]. In general, breast cancer has been reported to occur a decade earlier in Indian patients compared to their western counterparts. The average age of breast cancer patients has been reported to be 50–53 years in various population-based studies done in different parts of the country [10]. However in the current study the mean age of presentation was 47.84 years. This shows a trend of earlier presentation of almost 3 – 5 years in the study population.

Duct cell carcinoma was the most common histological subtype (148 cases) accounting for 85% of the cases. Mucinous carcinoma was the second most common, occurring in 7 cases (4%). In a study from New Delhi [11], the histo-morphological types seen in breast cancer patients indicates that invasive ductal carcinoma not otherwise specified (IDC NOS) was found to be the most common type (88%) followed by infiltrating lobular carcinoma (3.7%), colloid carcinoma (1.1%), ductal carcinoma in situ (DCIS) (1.1%), and metaplastic types (0.9%). Our study demonstrates a lower incidence of lobular carcinoma (2.3%) when compared to the New Delhi based registry and the study of Lakhani et al, 2012. This may be due to the fact that most of our patients presented in early to middle age while lobular carcinoma tends to occur in little elderly patients when compared to DCC. According to Lakhani et al, 2012, invasive lobular carcinoma is the second most common type of breast cancer and comprises 5 – 15 % of all breast cancers[12].

In breast cancer, where the use of systemic therapy has to be determined for every patient, the three main prognostic determinants used in routine practice are lymph node (LN) status, tumor size, and histologic grade. Invasive carcinomas are morphologically subdivided according to their growth patterns and degree of differentiation.

Histologic grading describes the microscopic growth pattern of invasive ductal carcinomas as well as cytologic features of differentiation. The most widely used histologic grading systems are based on criteria established by Bloom [13] and Bloom and Richardson [14] and Elston and Ellis [5]. The Nottingham modification of the Scarff-Bloom-Richardson grading system, also known as the Nottingham Grading System (NGS), has been recommended by various professional bodies internationally (World Health Organization [WHO], American Joint Committee on Cancer [AJCC], European Union [EU], and the U.K. Royal College of Pathologists).

The parameters measured are: (a) the extent of tubule formation; (b) nuclear hyperchromasia, pleomorphism, and size; and (c) mitotic rate. Each of the three elements is assigned a score on a scale of 1 to 3, and the final grade is determined from the sums of the scores. Histologic grade is traditionally expressed in three categories: scores 3 to 5, well differentiated (grade I); scores 6 to 7, intermediate (grade II); and scores 8 to 9, poorly differentiated (grade III).

It has been reported that grade 2 tumors comprise up to 60% of invasive breast cancers. In our study we found a significantly higher percentage i. e 81.61 % of grade II tumours. This Indian data differs with the data at a major cancer center in the city of Mumbai where 70% patients were reported as having grade III disease [15].

Numerous studies have demonstrated that patients with high-grade or poorly differentiated invasive duct carcinomas treated by mastectomy had a significantly higher frequency of axillary lymph node metastases and of 4 or more positive lymph nodes, that they developed more systemic recurrences, and that more of them died of metastatic disease than did women with lower grade tumors[16,17]. Nuclear and histologic grades have been shown to be useful predictors of prognosis for patients stratified by stage of disease, especially among those without axillary lymph node metastases [18].

Histologic grade was reportedly a prognostically significant factor in monitoring response to adjuvant chemotherapy and endocrine treatment for systemic recurrence [19, 20] It has been shown to be significantly related not only to the frequency of recurrence and death due to invasive ductal carcinoma, but also to the disease-free interval and overall length of survival after mastectomy regardless of clinical stage [21].

The measured gross size represented by the largest diameter of a mammary carcinoma is one of the most significant prognostic variables. Numerous studies have shown that survival decreases with increasing tumor size and that there is a coincidental rise in the frequency of axillary nodal metastases [21, 22]. Highest numbers of tumours were detected in the T2 stage i.e with size varying between 2 – 5 cms (67.24%). In decreasing frequency T3 > T1 > T4 stage tumours were observed. It has been proven without doubt that axillary lymph node status is the single most predictive factor for the outcome of breast carcinoma and there is a corresponding decline in survival as the number of involved lymph nodes increases [23]. More number of cases in our study population belonged to either N0 category or N1 category.

About half of all invasive carcinomas show lymphovascular invasion i.e presence of tumour cells within vascular spaces lined by endothelial cells. This finding is strongly associated with the presence of lymph node metastases. It is a poor prognostic factor for overall survival in women without lymph node metastases and a risk factor for local recurrence. 90 cases had lymphovascular invasion in our study accounting for 51.72%.

Conclusion

Nottingham Grading system is a simple, inexpensive, and routinely applicable way that provides an overview of the intrinsic biological characteristics and clinical behavior of the tumor, adding important information to other significant and time-dependent prognostic factors, such as LN status and size. Our study puts forth such histopathological prognostic factor data concerning breast carcinoma in a subset of Indian population. We emphasize on the role of a standardized reporting protocol in learning the trends of breast carcinoma, a malignancy that has a poor social awareness despite many recent advances in management.

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