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A Study of Clinicopathologic Spectrum of Carcinoma Breast

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Abstract

Introduction: Traditional models of breast cancer development are based on morphological studies and suggest the transition from a normal epithelial cell via hyperplasia and atypical hyperplasia to ductal carcinoma in situ. The risk for carcinoma increased with the rate of proliferation and atypia in breast biopsies. *Methodology:* In this study, collection of family history and interrogation with the patient forms an integral part. This was done by direct communication with the patient at the Pathology and Surgery departments, collection of details from the radiotherapy department records and by collecting filled up proforma from the patients by post. *Results:* It is clearly seen that nearly 78% of the tumours belonged to the higher grade –Grade 2 and 3, whereas low-grade tumours constituted only 22%.*Conclusion:* The lymph node positivity is a strong indication to make the public aware of this disease and to intensify the screening and surveillance programmes

Keywords: Breast Carcinoma; Clinical Profile; Pathological Profile.

Introduction

Breast cancer is one of the leading causes of cancer deaths worldwide. It accounts for 23% of all carcinomas in women and 14.1% of female cancer deaths. Incidence rates have continued to increase world wide, with an overall increase of 0.5% since 1990 [1]. Changes in the incidence rates are greatest in the developing countries.

In India an average of 80,000 women are diagnosed with carcinoma breast and 40,000 die every year, of this disease [2]. Although it is currently the second most common carcinoma among Indian women (19%), after carcinoma cervix (30%), in the urban registries like Delhi, and Bombay, carcinoma breast has overtaken carcinoma cervix in frequency. These data not only demonstrate the current health problem associated with carcinona breast in the Indian population, but also indicate that socioeconomic trends will lead to rapid increase in its distribution to the overall health burden.

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The frequency of this disease has prompted an invasive study of the risk factors involved and the morphological spectrum of the disease, so as to gain clues to its etiology as well as to identify modifiable risk factors that would be helpful for prevention strategies.

Traditional models of breast cancer development are based on morphological studies and suggest the transition from a normal epithelial cell via hyperplasia and atypical hyperplasia to ductal carcinoma in situ. The risk for carcinoma increased with the rate of proliferation and atypia in breast biopsies. But the only intraductal proliferation that can be considered as an obligate precursor to every breast cancer is carcinoma in situ [3,4]. This does not imply that very in situ case will progress to invasive cancer. There is no direct evidence that epithelial hyperplasia and atypical hyperplasia are precursors to carcinoma neither from histopathological nor epidemiological or molecular biological studies.

Methodology

Study was done on the mastectomy specimens

received in the histopathology division of Department of Pathology, MCH, during the study period.

In this study, collection of family history and interrogation with the patient forms an integral part. This was done by direct communication with the patient at the Pathology and Surgery departments, collection of details from the radiotherapy department records and by collecting filled up proforma from the patients by post. A detailed family history was collected with a standard proforma.

Only mastectomy specimens were included in the study. They were fixed in 10% formalin. Sections were obtained from the tumour proper nipple& areola, adjacent areas of the tumour, surgical margins and lymph nodes. The sections are stained with Haematoxylin and Eosin. These were studied in detail under light microscope. Pathological interpretation of the specimen was done as to the tumour size histological type and grade, presence of DCIS, associated fibrocystic disease, skin involvement, involvement of surgical margins and lymph node status.

Results

Table 1: Age distribution

Age	Cases	%
< 20 years	0	0
20-30	4	3
31-40	19	13
41-50	58	40
51-60	42	29
>60 yrs	22	15

Table 2: Morphological Sub typing

Histology Type	No. of cases
Infiltrating duct Carcinoma (NOS)	136
Lobular Carcinoma	1
Medullary Carcinoma	2
Mucinous Carcinoma	1
Squamous Carcinoma	1
Metaplastic Carcinoma	4

Table 3: *Classification according to grade*

Tumour size	No. of Cases	%
< 2 cm	5	4
2 to 5 cm	118	81
More than 5	22	15

Table 4: Tumour Size

Grade	No. of Cases	%
Grade 1	32	22
Grade 2	67	46
Grade 3	46	32

Table 5: Other associated features

Features	No. of cases
Ductal Carcinoma in situ	
Grade 1	11
Grade 2	6
Grade 3	15
	Total 32 (22%)
Fibrocystic disease of Breast	
Without atypia	16
With atypia	2
	Total 18 (12%)
Paget's Disease	5
Lymph node metastasis	64 (45%)

Discussion

The maximum number of cases is in the 41 – 50 age group - 40%. 29% of the tumours were in the 51 -60age group, 16% in the below 40 age group and 15% above 60 years. Statistical data for the previous 5 years of this department clearly shows that there is a steady increase in the incidence of breast cancer every year. It also appears that there is a shift in the age composition of these patients from >50 age group, to < 50 age group. The number of cases in the above 60-age group is declining. These findings show that the pattern of age distribution reaches maximum in the 4th and 5th decades and remains constant or declines thereafter. There are two reasons for such a pattern.

The first and foremost is the acceptance of the newer screening measures by the general public. The young females are aware of the importance of early detection. They do self-palpation and seek medical advice as soon as they detect a lump. The triple assessment method – clinical examination, mammography and FNAC, provides rapid diagnosis without invasive procedures. The second reason is the difference in pre and postmenopausal hormonal status. Estrogen induces proliferation of the ductal epithelium. Both endogenous and exogenous estrogen excess can result in carcinoma. After menopause, there is a quick fall in the estrogen level. This may reduce the cancer risk in postmenopausal women.

The Histological Classification

The largest single group was Invasive Ductal Carcinoma (NOS), which constituted 94% of the study group. This is comparable to the findings in other studies. Many of the subtypes like tubular carcinoma, papillary carcinoma etc was not seen in this study. There were 4 cases of metaplastic carcinoma. This constituted a considerably larger group (3%) when compared to other studies [5,6].

Histological classification has prognostic significance. IDC variants like tubular carcinoma, mucinous carcinoma, medullary carcinoma, secretory carcinoma and papillary carcinoma has good prognosis. It has been proved recently that the production of gel forming secretory mucins like MUC-2 and MUC-6 is responsible for the better prognosis of mucinous carcinoma [7]. This mucin acts as a barrier against cancerous extension.

The Grade of the Tumours

Grading was done following the Modified Bloom Richardson method, taking into account tubule formation, nuclear pleomorphism and mitotic counts.

It is clearly seen that nearly 78% of the tumours belonged to the higher grade –Grade 2 and 3, whereas low-grade tumours constituted only 22%. This data is clearly significant because grading is a powerful prognostic information and most of the studies so far done have shown a significant association between grade of the tumour and patient survival [8]. Survival worsens with increasing grade.

Classification Based on Tumour Size

Size of the tumour is an easily measurable, strong predictor of tumour dissemination and prognosis. It is also a criterion for the classification of 'Minimal breast carcinomas' which includes all in situ carcinomas irrespective of the size and all invasive carcinomas less than or equal to 1 cm in diameter. These patients have 75% 10-year survival rate in node negative cases [9,10].

In the present study, tumour size of majority of patients was between 2-5 cm (81%). While in 4% of the patients the tumour size was <2 cm, only 15% of the patients had tumour size more than 5 cm. This shows that most of the lesions are detected before they attain very large size. Patient has a considerable survival advantage, if the tumour is diagnosed before attaining a large size.

Lymph Node Metastasis

45% of the tumours of this study group were node positive. Lymph node metastasis is the single most important prognostic parameter.

The presence of lymph node metastasis alters the stage of the disease irrespective of the tumour size. The 10-year survival rate of node negative patients is around 70%. This falls to 25 -30% in node positive cases[11,12]. Small node negative tumours can be cured by less vigorous treatment.

In this study majority of the patients have a favorable tumoursize. But irrespective of that, the high percentage of lymph node positivity places them in the higher stage, poor prognostic group.

Associated Proliferative Lesions

In this study, 22% of the cases showed associated DCIS and The opinion regarding considering in situ lesions, as prognostic factors are variable. Some studies say that prominent DCIS around an invasive tumour conveys a better prognosis [15,16]. In the modern era,

breast conservation surgeries are getting more popularity. So, the detection of in situ lesions in the resected margins of wide excision specimens determines the recurrence rates. Fibrocystic disease, which is considered as a forerunner of malignancy, was present in only 12% of the patients in the present study group.

Early Onset Carcinoma Breast Cases

Age Group

The age limit below which a carcinoma should be called as an early onset carcinoma varies in different studies. It has not been clearly defined till now. In a study by SunitaSaxenaet al [17], all cases less than or equal to 40 years is taken as early onset cases.

In this study, all cases less than or equal to 40 years are included in the early onset category. 16% of the cases were of early onset type. The youngest age detected was 25 years. The mean age calculated is 35 years. Sunita Saxena [17] et al got 59% of the cases in their study group, as early onset type. When compared to that, the percentage of early onset carcinoma cases in our population is low. Geographic risk factors may alter the epidemiology of carcinoma breast cases in different parts of the country.

The Histological Characteristics

All the 23 cases were histological invasive ductal carcinoma (NOS) type. Other variants like medullary carcinoma, secretory carcinoma which are usually described in younger age group, were not identified in this study. No significant difference in histological patterns is described between early onset carcinomas and those in older age group. IDC (NOS) is the most common type described in both groups.

Majority of the cases were in the grade 2 category. This observation is similar to that seen in the older age group.

Associated in situ carcinoma is seen in 56% of the cases. Majority are high grade DCIS. According to Claus EB et al [18], an inverse relation is seen between the age of onset and carcinoma in situ risk. He found out that, those cases < 49 years of age had 2.1 times risk than controls. Cases older than 49 years had 1.5 times the risk of controls. In this study, the association of more cases with high grade DCIS, may be the result of progression from florid epitheliosis through in situ carcinoma into invasive carcinoma.

Histologically all the 5 cases were invasive duct carcinomas (NOS) type. It is the most common histological type described in all forms of hereditary case [19]. A higher percentage of medullary carcinomas are also described. But no other histologic type was seen in this study. According to HannealinaErolaet al [20], the distinct pathologic features of hereditary carcinomas are found only in patients less than 50 years of age. These distinct pathologic features are high incidence of medullary carcinomas, high-grade tumours, ER/PR negativity and p 53 mutations.

2 cases showed in situ carcinomas (grade 1 and 2) and in 2 cases fibrocystic disease was present. The results vary in different studies. In the pre BRCA era [21], a higher prevalence of proliferative lesions (35%) was reported in hereditary cases. According to Claus EB, the family history of breast cancer is an important risk factor for carcinoma in situ. Cases with DCIS or LCIS are more likely to have a history of breast cancer in first degree relative.

Recent studies suggest that familial breast cancer is associated with a different set of initiating events when compared to sporadic carcinomas. A lower prevalence of precursor lesions is seen hereditary cancers [22]. This is due to the acceleration of tumourigenesis in these cases. The environmental carcinogenesis step is bypassed and there is a quick progression of tumour cells through a low-grade phase into a higher grade.

Conclusion

- Comparatively younger age group females are also affected by this disease with much frequency than previous years.
- Nearly half of the study group has lymph node positivity at the time of diagnosis.

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