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STUDY OF EPITHELIAL CHANGES IN ADJOINING BREAST TISSUE OF MASTECTOMY SPECIMENS IN INFILTRATING DUCT CARCINOMA AND ITS CORRELATION WITH TUMOR SIZE AND GRADE

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ABSTRACT Many breast carcinoma probably arise in a multi-step fashion through a series of intermediate lesions i.e. ductal hyperplasia of usual type (HUT) to atypical ductal hyperplasia (ADH) to ducal carcinoma in situ (DCIS) and thereafter to invasive ductal carcinoma (IDC), each of which has a greater propensity of becoming malignant than the one that preceded it [1]. Keeping in mind the above, the study was undertaken to detect proliferative epithelial changes in the adjacent breast parenchyma in 50 mastectomy specimens of infiltrating duct carcinoma. Out of 50 cases, 25 cases showed ductal hyper plastic changes in the form of HUT (Mild or moderate or florid), and DCIS. Mild hyper plastic changes were seen in 20 cases (40%). Moderate duct hyperplasia was seen in 10 (20%) cases and florid duct hyperplasia was seen in 3 (6%) cases. Foci of DCIS were noticed in 10 cases. No ADH was observed in our study.

KEYWORDS : HUT (Hyperplasia of usual type), ADH (Atypical ductal hyperplasia), DCIS (Ducal carcinoma in situ), IDC (Invasive ductal carcinoma)

INTRODUCTION

Breast carcinoma ranks as the second common carcinoma in women in India. It accounts for approximately 100,000 new cases in Indian women every year [2]. Detection at an early stage improves the prognosis of breast carcinoma, almost to near curable state today with targeted therapeutic regimes. Despite major diagnostic and therapeutic innovations, the effect on mortality has been modest. One of the factors contributing to this limited success is our relative lack of understanding of natural history of the disease.

Many breast carcinoma probably arise in a multi-step fashion through a series of intermediate lesions i.e. ductal hyperplasia of usual type (HUT) to atypical ductal hyperplasia (ADH) to ducal carcinoma in situ (DCIS) and thereafter to invasive ductal carcinoma (IDC), each of which has a greater propensity of becoming malignant than the one that preceded it [1]. It must be inferred that the ductal epithelium, at some point undergoes a change to a preneoplastic character and subsequently to neoplastic one. A woman with conventional ductal hyperplasia has a slightly higher likelihood of developing invasive breast carcinoma (1.5-2.0 times) than a woman without hyperplasia does [3]. Atypical ductal hyperplasia carries a somewhat higher relative risk (about 4 times) [3] especially among premenopausal women [4]. A family history of breast cancer approximately doubles the number to about 9 times the background rate [4]. Both breasts seem equally likely to develop invasive carcinoma [5]. Finally, patients with ductal carcinoma in situ run a substantial risk of developing invasive carcinoma [5].

Keeping these views in mind, this study was undertaken to detect proliferative changes in adjoining breast parenchyma in mastectomy specimens of all cases of IDC.

MATERIAL AND METHODS

A total number of 50 cases of infiltrating duct carcinoma operated at a tertiary care centre were selected for this study during the period May 2014 - May 2016 at a tertiary care centre. Specimens of modified radical mastectomy (MRM) were grossed as per the standard procedure [6]. further to this, sections from each quadrant were taken preferably from areas which appeared firmer on palpation than rest of breast and areas showing whitish streaks. The sections were subjected to Haematoxylin and eosin stains. Tumor was assigned pathological stage (pTNM) as per the standardized TNM definitions. The features that were used in identification of the benign, atypical and malignant nature of the proliferative lesions in the adjoining breast tissue were as per the standard criteria [5].

OBSERVATIONS AND RESULTS

A total number of 50 patients of infiltrating duct carcinoma operated at a tertiary care centre were selected for this study. Majority of the tumors were Grade-III. Out of 50 cases, 25 showed Intraductal epithelial proliferations in the form of hyperplasia of usual type (Mild or moderate or florid), and ductal carcinoma in situ. On analysis of pattern of these epithelial proliferations, it was observed that variable degrees of mild hyper plastic changes were seen in 20 out of 25 cases. Moderate duct hyperplasia was seen in 10 cases and florid duct hyperplasia was seen in 3 cases. No atypical duct hyperplasia was observed in this study. Foci of duct carcinoma in situ were noticed in 10 cases in the adjacent breast.

Out of 50 cases of infiltrating duct carcinoma, there were no case of grade I and 22 cases in grade 2 and 28 in grade 3 categories. Out of 22 cases of IDC grade II, 8 cases showed hyper plastic epithelial proliferations. 17 out of 28 grade III tumors showed hyper plastic epithelial proliferations. It is seen that grade 2 tumor showed 36.3% epithelial proliferations in surrounding breast. As the grade increased, increased degree of epithelial proliferations were seen in the adjoining breast tissue.

Table 1 Relationship of histological grade of tumor with Proliferative changes

Histological grade	No. % of patients	Proliferative changes
IDC Grade 1	Nil -	- -
IDC Grade 2	22 (44 %)	8 (36.3%)
IDC Grade 3	28 (56%)	17 (60.7%)

The cases with tumor size between 2-5cm (25 cases) were maximum and 14 (56%) out of these showed epithelial changes in the surrounding breast parenchyma. Though the number of cases with tumor size less than 2cm were only four, all four of them showed epithelial changes. Detection rate of epithelial changes in surrounding breast tissue was lower for T2 (56%) and T3 (33.3%) tumors as compared to T1 tumors (100%). Number of sections showing epithelial proliferations of adjacent parenchyma also showed a similar trend. The difference was statistically analyzed using chi square (Yates corrected). For statistical analysis, the T1 and T2 tumors were combined into one group. The difference was

statistically significant ($p < 0.05$) indicating smaller tumors show more proliferative changes.

Table 2 Relationship of tumor size with proliferative changes

Tumor size	No of cases	No of cases showing proliferative changes	Total no of sections	Sections with proliferative changes
<2.0 cm	4	4 (100%)	16	10 (62.5%)
2 - 5 cm	25	14 (56%)	100	30 (30%)
>5cm	21	7 (33.3%)	84	13 (15.4%)

DISCUSSION

Infiltrating duct carcinoma is the most common type of breast carcinoma. As carcinogenesis is a complex multistep process, the strategy should be diagnosis of a precancerous stage.

Our study was a prospective study conducted to detect the rate of detection of ductal epithelial changes in adjoining breast parenchyma in cases of infiltrating breast carcinoma. These epithelial changes were then correlated with grade and size of the tumor. Our study demonstrated epithelial changes in 50% of patients of infiltrating duct carcinoma.

Out of 50 cases, 25 showed ductal hyper plastic changes in the form of hyperplasia of usual type (Mild or moderate or florid), and ductal carcinoma in situ. Our study was comparable to the study done by Silverberg et al [7] who also detected intraductal papillomatosis in 50% cases of infiltrating duct carcinoma. But Tellem [8] has a much higher percentage of detection of epithelial changes in his four quadrant study of breasts removed for carcinoma as he found cystic proliferative disease in the majority of cancerous breasts.

There are studies in literature [11] which quote the rarity of true atypical ductal hyperplasia and recommend search for unequivocal areas of DCIS whenever a diagnosis of ADH is contemplated. We agree in this regard with the author while differ from others [9]. We, in our study, adhered to criteria given by Page and Colleagues [5] to diagnose a lesion as ADH. Though, we found lesions appearing as atypical proliferations in 3 cases but they were finally categorized as low grade DCIS after studying other areas of the sections thoroughly.
In this study, the sectioning of adjacent breast parenchyma was done much away from tumor margin. It decreased the sampling error attributable to increased frequency of DCIS in immediate vicinity of tumor. We sampled all the 4 quadrants randomly by enlarge, though areas showing whitish streaks and firm on palpation than rest of breast were preferred when found in the mastectomy specimens.

Though in literature, there have been guidelines for random sectioning of UOQ routinely and four quadrant studies only on finding grossly abnormal and diseased areas such as whitish streaks, cysts and satellite nodules in mastectomy specimens [3]. We, in our study, found that foci of DCIS or florid HUT can be present in one or two quadrants only with remaining quadrants showing normal breast parenchyma. It was seen that study of four quadrants can detect high risk intraductal proliferations which otherwise deserve mentioning in the histopathology report and can be missed if only one or two sections of adjacent breast parenchyma are taken in grossing of mastectomy specimens.

In the present study, we found that epithelial changes are more common in higher grade tumors but in relatively smaller tumors (Table 1 & 2). It is similar to that of Silverberg et al [7] who detected smaller sized tumors and more favorable clinical staging prior to surgery in women showing fibrocystic dysplasia but differs from others (10). One explanation for this could be that women having these proliferative lesions which are often found with other components of fibrocystic disease seek frequent consultation and are followed up more frequently; therefore their tumors are picked up in relatively earlier stages.

CONCLUSION

The chance that a patient with invasive breast cancer will develop a carcinoma in the contra lateral breast is about 5 times that of a general population. It has been suggested that this unfavorable outcome can be predicted by presence of high risk epithelial proliferations often termed as atypical ductal hyperplasia and ductal carcinoma in situ in the adjacent breast parenchyma in cases of IDC. Four quadrant study of adjacent breast can increase the detection rate of high risk and precursor ductal proliferations which, in turn, can be useful in predicting the chances of development of carcinoma in the contra lateral breast subsequently and planning follow-up strategies for early detection of breast cancer in such patients. The histomorphological examination of adjacent breast parenchyma in mastectomy specimens is a simple and valuable method for stratifying the risk of carcinoma in contra lateral breast. Hence four quadrant study of adjacent uninvolved breast parenchyma is recommended as a standard protocol in all cases of IDC.

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