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Original Research Article

Proliferative fibrocystic lesions in association with carcinoma breast- Study of mastectomy specimens

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Abstract

Background: Breast cancer remains a global health problem with an increasing incidence. Proliferative breast diseases are recognized as one of the risk factors in the development of carcinoma. The study was undertaken to know the frequency of proliferative fibrocystic lesions in association with breast carcinomas in mastectomy specimens.

Material and methods: The present study included 100 cases of mastectomies for carcinoma breast at Kempegowda Institute of Medical Sciences, Bangalore from August 2010 to July 2013.

The tumor and the surrounding breast tissue were studied grossly and microscopically for any co-existing neoplastic and non neoplastic lesions like epithelial hyperplasia, cystic change, apocrine metaplasia, fibrosis and adenosis.

Results: The study included 100 cases of breast carcinomas. The predominant type of carcinoma (85%) was infiltrating ductal carcinoma-no specific type. Proliferative breast lesions were noted in 38 cases (38%), nonproliferative breast lesions in 27 cases (27%) and there were no changes in 35 cases (35%). Of 38 cases, proliferative lesions with atypia were noted in 20 cases and proliferative lesions without atypia were noted in 18 cases.

Conclusion: Proliferative lesions in the breast carry an increased risk of developing malignancies especially when there is atypia. Women, who have been diagnosed as having proliferative breast disease, require careful follow-up, with annual mammographic screening being mandatory for women with atypical hyperplasia.

Keywords: Carcinoma breast, Proliferative breast lesions, Epithelial hyperplasia, Papillomatosis, Fibrocystic lesions, Apocrine metaplasia.

1. Introduction

Breast cancer remains a global health problem with an increasing incidence. It is the most common carcinoma in women and accounts for 22% of all cancers in women[1].

Breast cancer is a diverse group of disease in terms of presentation, morphology and molecular profile. Understanding the relationship between histopathologic and molecular changes associated with an increased probability of developing invasive breast carcinoma is fundamentally important. Such an understanding may enable more accurate assessment of risk, individualization of therapy, identification of specific defects that can be therapeutically targeted to prevent development and progression of the disease[2].

Benign breast diseases are broadly classified as nonproliferative lesions, proliferative lesions without atypia and proliferative lesions with atypia[3]. Proliferative fibrocystic disease is one of the risk factors described[4].

Previous studies have shown that, relative to nonproliferative benign breast disease, women with proliferative lesions without atypia are at slightly increased risk of subsequent breast cancer, whereas women with proliferative lesions with atypia have a substantially higher risk[4-6]. Studies have shown that proliferative disease with atypia, carcinoma in situ [Lobular carcinoma in situ (LCIS) and Ductal carcinoma in situ (DCIS)] have high risk of developing invasive carcinoma than the nonproliferative breast changes[7].

Many histologic entities are included in the benign breast disease, the relevant lesions with respect to the risk of subsequent breast cancer are those which are of epithelial origin. These lesions include fibroadenoma, sclerosing adensosis, radial scar, solitary papilloma and hyperplasia with or without atypia[8-10].

Aim

The aim of this study was to know the frequency of associated lesions in the surrounding breast tissue and categorize the lesions.

2. Material and Method

The study was undertaken to determine the presence of changes in the surrounding breast tissue in carcinoma breast and included 100 cases of mastectomy specimens of carcinoma breast in the Department of Pathology, Kempegowda Institute of Medical Sciences, Bangalore from August 2010 to July 2013.Demographic data and relevant clinical details were noted from the case files.

The mastectomy specimens were fixed in 10% formalin. Specimen was measured, grossly examined and serially sectioned at 2cms interval. Tumor was grossly examined and samples were taken. The surrounding breast tissue was examined for any lesions. When present - site, size, extent, colour and consistency were noted and bits were taken. Even in the absence of obvious gross lesions in adjacent breast tissue, four or more bits were taken for histopathological examination.

The tissues were processed routinely and multiple sections of 4-5 micron thickness were obtained from paraffin blocks, stained with Hematoxylin and Eosin.

Sections from the tumor and adjacent tissue were studied in detail for any co-existing neoplastic or non-neoplastic lesions like epithelial hyperplasia, cystic change, apocrine metaplasia, fibrosis, adenosis and for the presence of nuclear atypia.

Epithelial hyperplasia

Epithelial hyperplasia is characterized by increase in the number of cells in relation to basement membrane. It is classified as mild, moderate and florid hyperplasia[11].

Mild - epithelial cell proliferation is three or four layers.

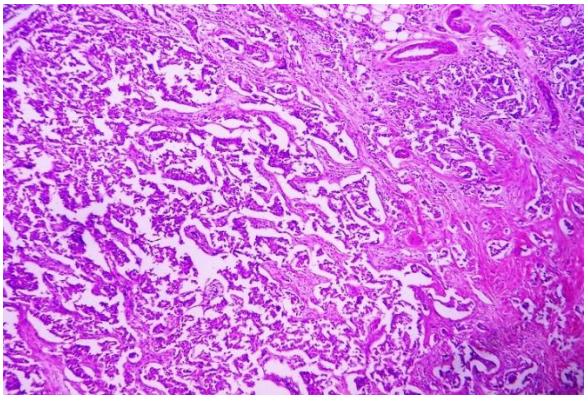
Moderate - epithelial cell proliferation filling nearly 70% of the lumen.

Florid - epithelial cell proliferation is more than 70% of lumen forming clefts, papillomas, arches and bridges. Hyperplasia with atypia - when nuclear pleomorphism is present.

3. Results

The study included 100 cases of breast carcinomas. The most common clinical presentation was lump in the breast. Some had complaints of pain and few presented with discharge from the nipple. The age of the patients ranged from 31-80 years. Most cases were seen in the age group of 41-60(65%). The predominant histological subtype of carcinoma observed was Infiltrating ductal carcinoma, no specific type (IDC, NST) (85 cases) (Figure 1).

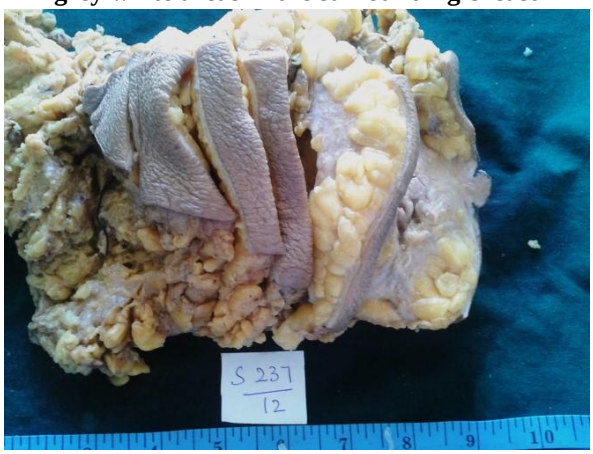
Figure 1: Microphotograph showing Infiltrating Ductal Carcinoma, No Specific Type (H&E x100)



There were 2 cases of Mucinous carcinoma, 2 cases of Intracystic papillary carcinoma, 3 cases of Invasive lobular carcinoma, 3 cases of Pleomorphic lobular carcinoma, 1 case each of Medullary carcinoma, Infiltrating adenosquamous carcinoma, Papillary mucinous carcinoma and 2 cases of High grade DCIS with microinvasion.

Grossly, the surrounding breast tissue showed grey white areas in 30 cases (30%) (Figure 2), tiny cysts in 3 cases and both cysts and grey white areas in 2 cases. Two cases showed multiple nodules. There were no gross changes in the remaining 63 cases.

Figure 2: Mastectomy specimen with tumor and grey white areas in the surrounding breast



Microscopic sections from the surrounding breast tissue showed proliferative lesions in 38 cases

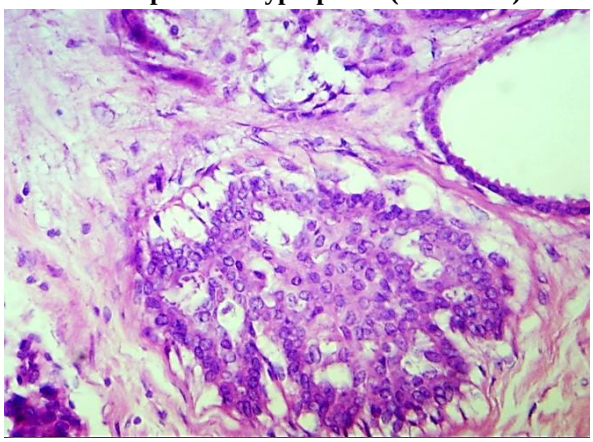
(38%) and nonproliferative lesions in 27 cases (27%). In the remaining 35 cases there were no changes noted microscopically.

Of these 38 cases of proliferative lesions, 20 cases showed atypia and 18 cases did not show atypia.

3.1 Proliferative lesions with atypia

The 20 cases of proliferative lesions with atypia in the surrounding breast tissue had moderate epithelial hyperplasia in 9 cases and florid epithelial hyperplasia in 11 cases (Figure 3).

Figure 3: Microphotograph showing ducts with florid epithelial hyperplasia (H&Ex400)



Six of 9 cases with moderate hyperplasia and all 11 cases of florid hyperplasia were associated with Infiltrating ductal carcinoma, no specific type (IDC, NST). Two cases of moderate hyperplasia with atypia were associated with High grade DCIS with microinvasion. One case was associated with Intracystic papillary carcinoma.

3.2 Moderate epithelial hyperplasia with atypia

In the 9 cases which showed moderate epithelial hyperplasia with atypia also had papillomatosis in 3 cases (Figure 4) and columnar cell lesions (CCLs) in 3 cases (Figure 5), of which 2 had columnar cell change (CCC) and 1 case showed columnar cell hyperplasia (CCH).

Figure 4: Microphotograph showing ducts with papillomatosis (H&Ex100)

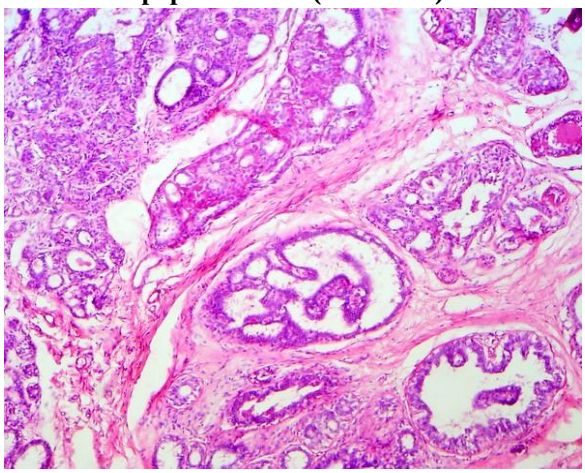
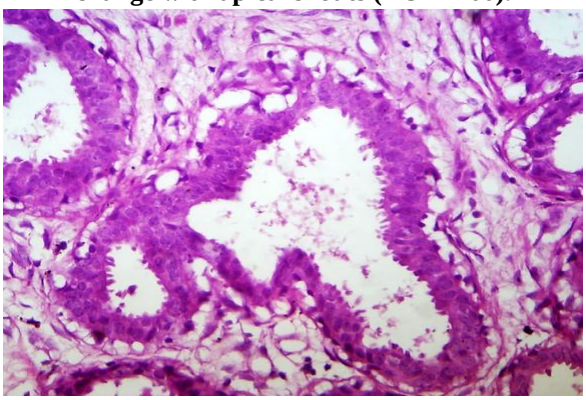
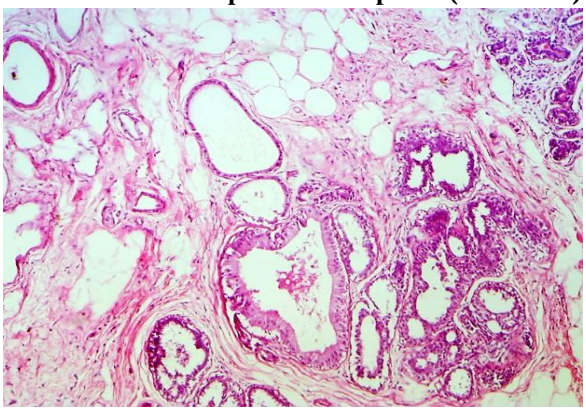


Figure 5: Microphotograph showing columnar cell change with apical snouts (H&Ex400).



Apocrine metaplasia (Figure 6), sclerosing adenosis and cystic change were noted in these cases along with epithelial hyperplasia.

Figure 6: Microphotograph showing cystically dilated ducts with apocrine metaplasia (H&Ex100)



3.3 Florid epithelial hyperplasia with atypia

Among eleven cases which showed florid epithelial hyperplasia with atypia, 6 cases had foci of DCIS and 1 case showed CCC. All these cases were seen in IDC (NST). One case was associated with Paget's disease in addition.

3.4 Proliferative lesions without atypia:

Eighteen of 38 cases of proliferative lesions showed only epithelial proliferation and no atypia. Ten cases showed mild epithelial hyperplasia, 5 cases showed moderate and 3 cases showed florid epithelial hyperplasia without atypia. Three of these cases showed CCC.

Fibrosis, cystic change and apocrine metaplasia(fig 6) were noted in these cases along with epithelial hyperplasia. Four cases showed focal fibroadenomatoid areas.

Three cases of Invasive lobular carcinoma, 3 cases of Pleomorphic lobular carcinoma,2 cases of Mucinous carcinoma and 1 case of Medullary carcinoma diagnosed histologically did not show any changes in the surrounding breast tissue grossly and microscopically.

4. Discussion

As breast cancer being the most common cancer among women in India and many regions of the world, constant study on proliferative fibrocystic disease are being done to note the degree of risk of these proliferative diseases in developing breast cancer.

The age range in 100 cases of breast carcinomas was 31-80 years. Fifty one (51%) women with breast carcinoma were seen in the age group of 31-50 years in our study. This finding corresponds to the statistical study of breast carcinoma cases in Bangalore where the incidence of breast carcinoma was 54% in the age group of 25-50 years[12].

Twenty five years back, out of every 100 breast cancer patients, 2% were in 20-30 years age group, 7% were in 30-40 years age group and 69% of the patients were above 50 years of age. Presently, 4% are in 20-30 years age group, 16% are in 30-40 years age group, 28% are in 40- 50 years age group. So, almost 48% patients are below 50 years. An increasing number of patients are in the 25-40 years of age group[12]. This showed the age shift of breast carcinomas from the age 60 -70 years to 30 - 40 years of age.

The predominant histological subtype of carcinoma diagnosed was infiltrating ductal carcinoma-no specific type (IDC, NST) (85%).

4.1 Microscopic lesions in the surrounding breast tissue

In our study of 100 cases of breast carcinomas, 38 cases (38%) showed proliferative lesions and 27 cases (27%) showed nonproliferative lesions in the surrounding breast tissue. There were no changes in the remaining 35 cases (35%). London SJ *et al*.[5] did a prospective cohort study where the cases were women with breast cancer who had a prior biopsy for benign breast disease. Controls were randomly selected and matched on year of biopsy and year of birth from among women in the cohort who had a benign breast biopsy but who did not develop breast cancer. They had included 121 cases and 488 controls. They had observed nonproliferative lesions in 46 cases (38.0%), proliferative lesions without atypia in 48 cases (39.6%) and proliferative lesions with atypia in 27 cases (22.3%). The relative risks (RR) for breast cancer, relative to women with no proliferative disease were 1.6 for proliferative disease without atypia (95% confidence interval (CI), 1.0 to 2.5) and 3.7 for atypical hyperplasia (95% CI, 2.1 to 6.8). Breast cancer risk was more strongly associated with atypical hyperplasia among premenopausal women (RR=5.9; 95% CI, 2.9 to 13.2) than postmenopausal women (RR= 2.3; 95%CI, 0.9 to 5.9). Hartmann LC *et al*.[13] in their study identified all women who were diagnosed of benign breast disease and calculated the relative risk by comparing the number of observed breast cancers with the number expected. The follow up study of 9087 women showed nonproliferative lesions in 6061 cases (66.6%), proliferative lesions without atypia in 2690 cases (29.6%) and atypical hyperplasia in 336 cases (3.6%). They concluded that RR associated with atypia was 4.24 (95% CI, 3.26 to 5.41), as compared to 1.88 (95%CI, 1.66 to 2.12) for proliferative changes without atypia and 1.27 (95% CI, 1.15 to 1.41) for nonproliferative lesions.

In the present study, nonproliferative lesions in 27 cases, proliferative lesions without atypia in 18 cases and proliferative lesions with atypia in 20 cases were noted in the breast tissue specimens with carcinoma.

4.2 Nonproliferative lesions:

The 27 cases of nonproliferative lesions noted in the surrounding breast tissue showed fibrosis in 15 cases, adenosis in 9 cases, cystic change in 13 cases, apocrine metaplasia in 4 cases, columnar cell change in 3 cases and calcification in 3 cases.

Cystic changes in the breast are common that various autopsy studies done randomly showed nearly 50% of the women have cystic changes[14]. In a study of unsuspected cystic disease found at autopsy in women dying of other causes, the average incidence found by various investigators was 58.5%. Cystic disease was bilateral in 43%, gross cyst were seen in 21%, coexisting gross and microscopic cysts were seen in 58.3% and cystic disease with epithelial hyperplasia was seen in 30.6% [14]. Sloss *et al*.[15] studied the breasts in 100 consecutive autopsied women of all ages who did not have any history of breast complaints, found microscopic cysts in 63; gross cysts were in 31 of the 63. Cysts were bilateral in 34. Intraductal hyperplasia was seen in 33 instances – 28 in the right breast and 24 in left breast. The size of the breast did not affect these findings.

Clinically occult proliferative disease and carcinoma were found in a study done on reductionmammaplasty (RM) specimens. Ishag *et al*.[16] in their study on 560 breast tissues removed during reduction mammaplasty (503 bilateral and 57 unilateral) noted pathologic changes in 338 cases(60.4%). Unsuspected carcinomas (small invasive carcinomas, 3; ductal carcinoma *in situ*, 1) were found in 4 cases (0.7%). Atypical ductal and/or atypical lobular hyperplasia were identified in 8 cases (1.4%). Lesions associated with a mildly increased carcinoma risk (moderate/florid ductal hyperplasia, sclerosing adenosis, and papilloma) were identified in 52 cases (9.3%).

Other findings included fibrocystic changes, fibrosis, mild ductal hyperplasia, fibroadenoma, and adenosis. They concluded that histopathological examination of the RM specimen should be done routinely as it provides important clinical information.

4.3 Proliferative lesions:

4.3.1 Epithelial hyperplasia (EH)

Risk for Breast cancer among women with Benign Breast Disease by presence of Epithelial Hyperplasia and Atypia. McDivitt RW *et al*.[17] analyzed data from population based, case-control study of women aged 20- 54 years with newly diagnosed breast cancer and control subjects randomly selected from the general population. Biopsy slides of 433 women with breast cancer and 261 control subjects, all of whom had a history of biopsy for benign breast disease (BBD), as to the presence of epithelial hyperplasia, atypia and other histological findings. Their study showed that in women with biopsies who were confirmed of Benign Breast Disease (BBD), the risk of developing breast cancer was 1.7 times that for women with no history of surgery for BBD. The women at highest risk for breast cancer were those with hyperplasia with moderate or marked atypia. For these women, the risk for breast cancer was 2.6 times that for women without BBD.

In the present study of 100 cases of mastectomy specimens that were histologically diagnosed as carcinoma breast, 35 cases (35%) did not show any changes, 65 cases (65%) had BBD. Proliferative lesions (epithelial hyperplasia) were seen in 38 cases (38%) and nonproliferative lesions in 27 cases (27%).

Of 38 cases, 20 cases had atypia and were associated with Infiltrating ductal carcinoma, no specific type. Of these 20 cases of proliferative lesions with atypia, 11 cases showed florid epithelial hyperplasia with atypia of which 6 cases had DCIS, 2 cases showed papillomatosis, 1case each showed CCC and apocrine metaplasia. Fibrosis and adenosis were noted in all these cases. Sclerosing adenosis in 2 cases, cystic change in 6 cases were noted.

4.3.2 Papillomatosis

R. Ali-Fehmi[18] in a study of 28 patients with breast lesions characterized by presence of multiple papilloma (MP) found atypical hyperplasia (AH) in 12 of 28 cases. DCIS associated with MP was typically low grade (17 of 20) and arose from areas within or immediately adjacent to preexisting benign lesions. They concluded that the frequent association with ADH, ALH/LCIS, malignant lesions and bilaterality imply that MP may represent a step in the progression of a precursor lesions to papillary carcinoma.

In the present study papillary lesions were noted in 5 cases. Four cases were associated with IDC, NST and one case was associated with intracystic papillary carcinoma.

4.3.3 Cystic disease

Davis HH *et al*.[14] studied the type of cystic disease associated with carcinoma in 327 cases and noted epithelial hyperplasia in 30.5% of cases. In the present study, we observed epithelial hyperplasia in 38% of cases.

4.3.4 Flat epithelial atypia (FEA or CCC or BDA)

Liebl *et al*.[19] in their study of 111 excisional breast biopsy specimens which had lobular neoplasia (LN), but did not have dutal carcinoma in situ (DCIS) or invasive carcinoma revealed 87% coexistence of LN and FEA. Abdel-Fatah TMA *et al*.[20] in their study of 147 tumor cases found 76 cases of pure tubular carcinomas (TC) had associated CCLs with the majority showing FEA. ADH/DCIS and TC was present in 89% patients. Co localization of CCH, ADH/DCIS and TC was seen in 85% patients.

In the present study, CCLs was seen in 10 cases (10%), of which 9 cases showed CCC which were associated with IDC (NST) in 8 cases and High grade DCIS with microinvasion in 1 case. CCH was seen in 1 case which was associated with IDC (NST). Six cases of lobular carcinomas did not show any changes in the surrounding breast tissue. This can be probably attributed for small number of lobular carcinomas in this study.

5. Conclusion

Breast carcinomas are increasing in incidence in the younger age group with 51% of cases seen in <50 years of age. The most predominant histological type of carcinoma was Infiltrating ductal carcinoma, no specific type (IDC, NST) (85%).

Proliferative lesions in the breast are recognized as one of the risk factors in developing breast carcinoma. We noted the frequency of these lesions associated with breast carcinoma (as 38%). Almost all were seen associated with infiltrating ductal carcinoma-no specific type (IDC, NST).

All cases of proliferative lesions in the breast carry an increased risk especially when there is atypia. Women who have been diagnosed as having proliferative breast disease require careful follow-up, with annual mammographic screening being mandatory for women with atypical hyperplasia.

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