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Columnar cell lesions and Flat epithelial atypia in mastectomy specimens – An institution based study in North Kerala

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Abstract

Introduction: Columnar cell lesions (CCL) are thought to be low grade precursor lesions of breast cancer. The prevalence of these lesions has not been well documented in the published literature. Data regarding the same in Indian scenario is also scarce. The present study attempts to document the extent and pattern of distribution of CCL and other proliferative breast lesions in the mastectomy specimens received in our department.

Objectives: To find the prevalence of CCL in the mastectomy specimens and to find out the prevalence of various known risk factors in the study population.

Materials and Method: The patients who underwent mastectomy or breast conservation surgery for carcinoma breast during December 2012 to May 2014 were included in the descriptive study conducted in the Department of Pathology, Government Medical College, Kozhikode. After taking informed consent clinical details were collected from the patient. Mastectomy specimens were evaluated for the presence of proliferative breast lesions. The variables were statistically analyzed using SPSS version 16.0. Results 60 patients were included in the study. Most of the patients belonged to the age group of 51-60 years. 16 cases were premenopausal and rest 44 postmenopausal. Histological grade 2 was most common and majority of our cases presented in TNM stage 2a. 56.7% cases showed proliferative breast lesions. DCIS was the commonest, seen in 40% cases. CCL were seen in 33.3% cases. No statistically significant relation was obtained between proliferative breast lesions and tumor grade, stage, nodal status, fibrocystic change, triple negativity of the tumor and menopausal status of the patient. As tumor grade progressed, triple negative tumors also increased and this was statistically significant ($p<0.05$)

Conclusion: In our study columnar cell and other proliferative breast lesions were seen in 56.7% mastectomies but CCL did not show any significant relation to menopausal status of the patient, tumor grade, tumor stage, nodal status, fibrocystic breast disease and triple negativity of the tumor.

Keywords: Columnar Cell Change, Columnar Cell Hyperplasia, Columnar Cell Lesion, Flat Epithelial Atypia, North Kerala

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Introduction

Invasive breast cancer is the most common carcinoma in women which accounts for 22% of all female cancers worldwide and 27% of all cancers in India.[1,2] Columnar cell changes have been known for many years. There is a renewed interest in these lesions as they now come across the pathologist's microscope frequently as a result of abnormal calcifications seen on screening mammography biopsied more often.

A simple classification of CCL was put forward by Schnitt and Vincent-Salomon in 2003.[3,4] Nowadays a practical classification system, which divides columnar cell lesions in three broad categories as columnar cell change (CCC) , columnar cell hyperplasia (CCH) and columnar cell change/hyperplasia with cytological atypia has been adopted.[5] The World Health Organization has proposed the term flat epithelial atypia (FEA) for columnar cell change/ hyperplasia with atypia.

All forms of columnar alterations show up-regulation of Estrogen receptor (ER) compared with adjacent normal breast lobules, with diffuse strong immunostaining with antibodies directed against ER-α. The immunohistochemical profile of CCL resembles that seen in ADH and low-grade DCIS and contrasts with that seen in benign epithelial hyperplasia, delineating CCL as a clonal proliferation and possibly a precursor lesion of low-grade malignancy.[6]

Evidence is gathering that CCLs may be biologically significant, possibly representing a very early stage in the evolution of low-grade DCIS and invasive carcinoma. This information comes from observational studies reporting the coexistence of CCLs with more advanced lesions, a small number of longitudinal patient follow-up studies, immunohistochemical and molecular genetic profile studies.[6-9]

There is emerging evidence that the spectrum of columnar cell lesions are related morphologically, cytologically, and by molecular alterations to ADH and DCIS. Hence they are considered to be precursor lesions in the low-grade estrogen-dependent pathways of ductal/ lobular neoplasia.

In our study we tried to find out the prevalence of these proliferative breast lesions in the mastectomy specimens.

Materials and Method

The study was a descriptive study of patients diagnosed with carcinoma breast during December 2012- May 2014 conducted in the Department of Pathology, Government Medical College, Kozhikode. Patients who had undergone mastectomy or breast conservation surgery for carcinoma breast proved by FNAC, trucut biopsy, incision or excision biopsy, during the study period were included in the study**.** Patients who underwent neo-adjuvant chemotherapy were excluded.

Ethical clearance was obtained from the Hospital Ethical Committee.

After taking informed consent relevant clinical information collected by direct interview of the patient. Details collected include name, age, menstrual and reproductive history, treatment history, previous history of breast disease and family history.

Mastectomy specimens of the patients received in our pathology department were grossed within 3 hours and fixed in 10% formalin. After adequate fixation, bits were taken from the tumor, surgical margins, nipple and 5 bits from adjacent breast tissue representing all quadrants. Histopathological features of the tumor studied including tumor size, tumor grade by Modified Bloom- Richardson grading, pathological tumor staging as per AJCC TNM staging of breast cancer 7th edition guidelines.

Adjacent breast tissue changes were noted. Columnar cell change defined as acini lined by one or two layers of columnar epithelial cells with uniform ovoid nuclei oriented perpendicular to basement membrane with evenly dispersed chromatin, inconspicuous nucleoli and infrequent mitotic activity.[3,5] Columnar cell hyperplasia defined as acini lined by more than two layers of columnar epithelial cells with cytological features similar to CCC.[3,5] FEA, ADH, DCIS, sclerosing adenosis, usual ductal hyperplasia (UDH) as per WHO tumours of breast and female genital system 4th edition definition.

The variables were analyzed using standard analytical techniques with SPSS version 16.0 for Windows. The associations between study variables were analyzed using Chi-square test and p values <0.05 were considered significant.

Results

A total of 60 patients who underwent mastectomy for carcinoma breast were included in the study. Age of the patients ranged from 32 to 78 years, the mean being 53 years. The maximum number of patients belonged to the age group 51 to 60 years. Majority of the tumor were in the upper outer quadrant of breast (36 cases). Of the total 60 cases, 16 were in pre-menopausal women and rest of the 44 post-menopausal. 3 of the patients were unmarried and 8 were nullipara. Among them, 2 were pre-menopausal and rest 6 post-menopausal. 2 cases with positive family history were both seen in postmenopausal patients.

Infiltrating duct carcinoma NOS was the most common type constituting 56 (93%) cases. There were 2 cases of Paget's disease and one case each of medullary carcinoma, invasive cribriform carcinoma, intraductal papillary carcinoma. 41 cases were grade 2 tumors. Pathological TNM staging was done. 15.4% cases were in stage 1, 34.6% in stage 2a, 19.2% in stage 2b, 21.2% in stage 3a and 9.6% in stage 3b. None of the patients had stage 4 disease.

Proliferative breast lesions: Lesions observed in the study were CCC, CCH, FEA, UDH and ADH (taken together as ductal hyperplasia for analysis), DCIS and sclerosing adenosis. Proliferative breast lesions were seen in 56.7% of cases. Table 1 shows the prevalence of these lesions in the sample. The proliferative breast lesions were compared with the menopausal status of the patients (Table 2).The proliferative breast lesions did not show any statistically significant relation to the tumor grade (Table 3), tumor T stage (Table 4), tumor nodal status (Table 5).

Table 1: Prevalence of proliferative lesions in the study sample

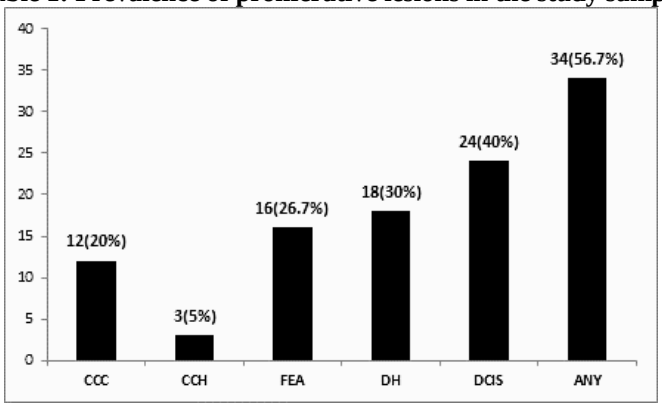

Table 2: Comparison of various proliferative breast lesions between pre-menopausal and post-menopausal patients

	N	Prevalence- Number (%)					
		CCC	CCH	FEA	DH	DCIS	ANY
Premenopausal	16	4(25.0)	1(6.3)	5(31.3)	5(31.3)	8(50.0)	10(62.5)
Postmenopausal	44	8(18.2)	2(4.5)	11(25.0)	13(29.5)	16(36.4)	24(54.5)
p		0.4007	0.6129	0.4295	0.5675	0.2547	0.4018

Table 3: Distribution of proliferative breast lesions according to tumor grade

Tumor Grade	N	Prevalence- Number (%)					
		CCC	CCH	FEA	DH	DCIS	ANY
1	7	2(28.6)	1(14.3)	2(28.5)	2(28.6)	3(42.8)	3(42.9)
2	41	6(14.6)	1(2.4)	10(24.4)	11(26.8)	18(43.9)	24(58.5)
3	7	3(42.8)	1(14.3)	3(42.8)	5(71.4)	3(42.8)	5(71.4)
p		0.1878	0.2417	0.5961	0.0651	0.9977	0.5536

Note: 5 cases had underwent excision biopsy from outside centres and showed no residual tumour, hence grading and tumor T staging done in 55 cases.

Table 4: Distribution of proliferative breast lesions according to tumor T stage

Tumor T Stage	N(54)	Prevalence – Number (%)					
		CCC	CCH	FEA	DH	DCIS	ANY
pT1	13	2(15.4)	1(7.7)	4(30.8)	4(30.8)	5(38.5)	6(46.2)
pT2	34	9(26.5)	2(5.9)	10(29.4)	14(41.2)	18(52.9)	24(70.6)
pT3	5	1(20.0)	0(0.0)	1(20.0)	0(0.0)	0(0.0)	2(40.0)
pT4	3	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
p		0.7309	0.9119	0.7956	0.2141	0.0795	0.0933

Table 5: Distribution of proliferative breast lesions according to tumor nodal stage

Tumor Nodal Stage	N(58)	Prevalence- Number (%)					
		CCC	CCH	FEA	DH	DCIS	ANY
pN0	30	7(23.3)	2(6.7)	8(26.7)	8(26.7)	8(26.7)	15(50.0)
pN1	14	1(7.1)	0(0.0)	3(21.4)	4(28.6)	7(50.0)	8(57.1)
pN2	11	2(18.2)	1(9.1)	1(9.1)	4(36.4)	6(54.5)	7(63.6)
pN3	3	2(66.7)	0(0.0)	3(100.0)	2(66.7)	2(66.7)	3(100.0)
P		0.1328	0.7036	0.0157	0.5255	0.1972	0.3827

Note: 2 cases were conservative mastectomies without lymphnode dissection.

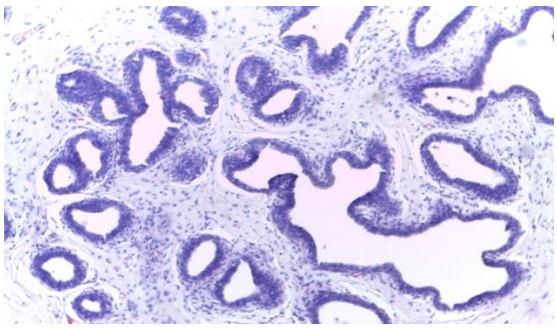

Fig. 1: Columnar cell change- H& E stained section 20x

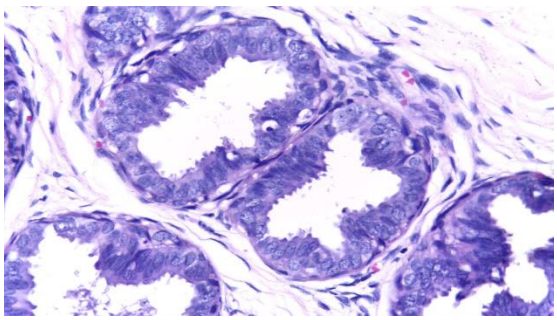

Fig. 2: Columnar cell change- H& E stained section 40x

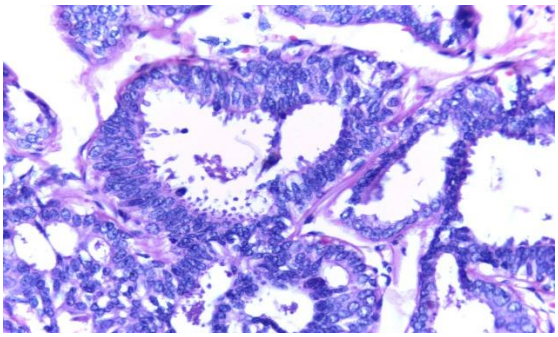

Fig. 3: Columnar cell hyperplasia- H& E stained section 40x

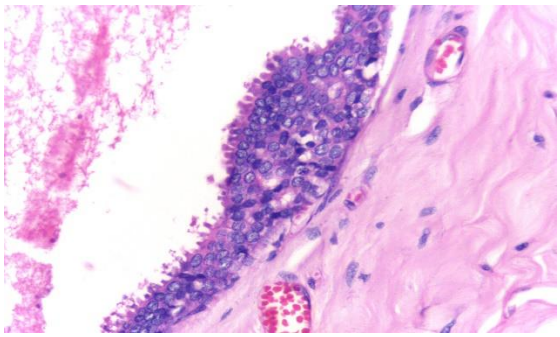

Fig. 4: Flat epithelial atypia- H& E stained section 40x

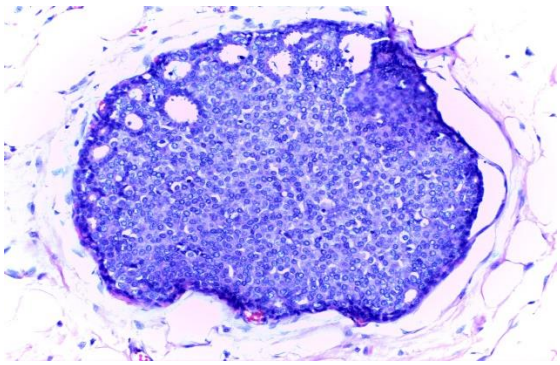

Fig. 5: Atypical ductal hyperplasia- H& E stained section 20x

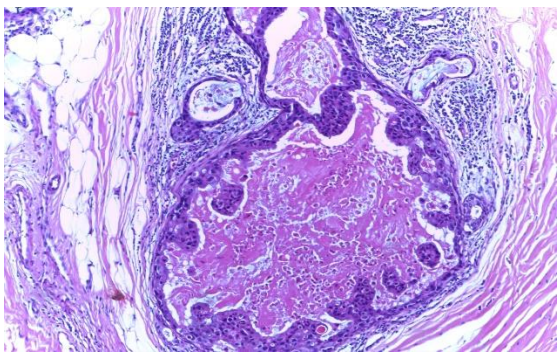

Fig. 6: DCIS highgrade with comedonecrosis- H& E stained section 20x

Discussion

A total of 60 patients who underwent mastectomy for carcinoma breast were included in the study. These patients hadn't received any neo-adjuvant chemotherapy. The maximum number of patients belonged to the age group 51- 60 years similar to studies reported from India and other Asian countries.[10,11] Of the total 60 cases 16 were in pre-menopausal women and rest of the 44 post-menopausal. We had more number of postmenopausal breast cancers which is similar to other Indian studies.[10,11]

Comparison of menstrual, child birth and breast feeding parameters was done between pre-menopausal and post-menopausal patients. The mean age of occurrence of breast cancer was 39.8 years in premenopausal and 58.3 in postmenopausal patients. The average years of breastfeeding differed significantly between the 2 groups (4 and 5.4 years respectively). Increased duration of breast feeding might have possibly delayed the occurrence of breast cancer in the postmenopausal group.

Familial pattern of breast cancer is low in numerous Indian studies but is much higher in western literature. In our study family history was obtained only in 2 cases (3%). Another study from North India had only 5% of cases with a family history of breast cancer.[12]

Infiltrating duct carcinoma- Not otherwise specified (IDC-NOS) was the most common histological type accounting for 93% cases. Pathological TNM staging was done in 52 cases. Most of our cases belonged to stage 2a (34.6%), followed by 3a (21.2%). This is different from the observations in some other Indian studies. Saxena et al found maximum cases were having stage 3b (35.2%) followed by 3a (27.1%).[11] Aruna et al reported similar finding with 75% cases having stage 3 disease.[10] Our patients generally presented at an earlier stage and probably is reflective of the higher penetration of education and health care in the state.

Proliferative changes in the mastectomy specimens were recorded in all the 60 cases. They were seen in 56.7% of cases. DCIS was the commonest seen in 40% cases. FEA, CCC, CCH in 26.7%, 20% and 5% respectively. Comparison of various proliferative breast lesions between pre-menopausal and post-menopausal patients was done. Though all proliferative lesions showed a trend of being higher in the postmenopausal group, it was not statistically significant. Distribution of various proliferative breast lesions with tumor grade and pathological T stage showed no statistical significance. Demiralay et al had compared columnar cell lesions in different tumor grades and found no significant difference.[13] Distribution of lesions according to pathological nodal status showed a significant p value< 0.05 obtained with FEA and nodal stage distribution.

Conclusion

In our study columnar cell and other proliferative breast lesions were seen in 56.7% mastectomies. DCIS was the commonest, seen in 40% cases. FEA, CCC, CCH were seen in 26.7%, 20% and 5% respectively. The proliferative breast lesions did not show any significant relation to menopausal status of the patient, tumor grade, tumor stage and nodal status.

The small sample size is a limitation in this study. More studies are needed to elucidate the true nature of columnar cell lesions.

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