Histopathological Study of the Relationship of Columnar Cell Lesions to Carcinoma Breast

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ABSTRACT

Introduction: Columnar cell lesions (CCLs) of the breast comprise a spectrum of benign to atypical entities that have in common variably dilated terminal duct lobular units lined by columnar epithelial cells with prominent apical cytoplasmic snouts. They are increasingly being encountered in breast biopsies because their associated microcalcifications are detected on mammographic screening. Current study aimed to know the proportion and significance of columnar cell lesions seen along with carcinoma breast.

Material and methods: Excision biopsy specimens of the breast which included both lumpectomies and mastectomies were studied in the department of pathology. Post-chemotherapy specimens were excluded from the study.5 sections each were taken from adjacent breast tissues and studied for columnar cell lesions after staining with hematoxylin, and eosin.100 cases were included in this study.

Results: Majority of the cases were diagnosed as IDC grade 2. One or the other columnar cell lesions were seen in the majority of invasive ductal carcinomas. CCLs may be characterized by a single layer of columnar cells (columnar cell change [CCC]), multiple layers with stratification and apical tufting (columnar cell hyperplasia [CCH]), or monomorphic cells with cytologic atypia (flat epithelial atypia [FEA]). The differentiation between CCC, CCH, and FEA is clinically significant: CCC and CCH are considered benign lesions, whereas FEA can be associated with, and even a precursor to, low-grade ductal carcinoma in situ and atypical ductal hyperplasia. Of the total 12 cases of grade 2 IDC, 8 cases (66.6%) showed columnar cell change, 4 of them showed columnar cell hyperplasia (33.3%) and 9 of them showed both flat epithelial atypia and ductal carcinoma in-situ changes (75%).

Conclusion: A consistent correlation exists between columnar cell lesions and Carcinoma Breast which is evidenced by the presence of such lesions in diagnosed cases of carcinoma. Since columnar cell lesions represent a significant precursor for carcinoma breast, a multidisciplinary modality of approach will help to detect these lesions much earlier and will prove worthwhile

Keywords: CCL - Columnar Cell Lesions, CCC - Columnar Cell Change, CCH - Columnar Cell Hyperplasia, FEA - Flat Epithelial Atypia, DCIS - Ductal Carcinoma in Situ, IDC - Infiltrating Duct Carcinoma

INTRODUCTION

Cancer breast has replaced carcinoma cervix as the leading cause of carcinoma in females in all urban PBCR's except Chennai. Columnar cell lesions (CCLs) of the breast comprise a spectrum of benign to atypical entities that have in common variably dilated terminal duct lobular units lined by columnar epithelial cells with prominent apical cytoplasmic snouts.[1,2] They are increasingly being encountered in breast biopsies because their associated microcalcifications are detected on mammographic screening.[2] CCLs present a new challenge in breast pathology. Many are benign histologically and biologically, others display cytological atypia, and yet others show both cytological and architectural alterations that place them into the category of ductal carcinoma in situ (DCIS).[3,4] CCC is the simplest form of CCL and is characterized by enlarged terminal duct lobular units (TDLUs) with variably dilated acini that may have an irregular contour. CCC consists of one to two layers of columnar epithelial cells that have uniform ovoid nuclei oriented perpendicular to the basement membrane and that have no conspicuous nucleoli. Apical cytoplasmic blebs, or snouts, are often present at the luminal surface of the cells, and flocculent secretions may be present in the lumina of the acini. CCC and apocrine metaplasia are both characterized by apical snouts; however, in apocrine metaplasia, the cytoplasm is more abundant and eosinophilic.[5]

Current study aimed to know the proportion and significance of columnar cell lesions seen along with carcinoma breast.

MATERIAL AND METHODS

This Observational Study was conducted in the Department of pathology, Government medical college, Kottayam. Excision biopsy specimens of breast received in the department of Pathology which included both lumpectomies and mastectomies. Post-chemotherapy specimens were excluded from the study. All specimens were received in 10% formalin and processed by paraffin embedding and blocks cut serially into sections of 5-micron thickness. All sections were stained by hematoxylin and eosin. 5 sections

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each were taken from adjacent breast tissues and studied for columnar cell lesions.

RESULTS

100 cases were included in this study, the majority of the patients in our study were in the age group between 45 to 55 years (34%). Only 2 patients were their under 35 years of age while 8 of them were above 75 years. Tumour typing were done and grading of invasive ductal carcinomas was done according to Bloom Richardson grading system

Of the total 100 cases studied, 59% comprised tumors belonging to invasive duct carcinoma not otherwise specified (IDC NOS) grade 2, 20% were of IDC grade 3 and IDC grade 1 comprised 12%. The remaining morphological types together constitute 9%, among which included lobular carcinoma, mucinous, metaplastic and invasive papillary carcinomas. Of the total 12 cases of grade 2 IDC, 8 cases (66.6%) showed columnar cell change, 4 of them showed columnar cell hyperplasia (33.3%) and 9 of them showed both flat epithelial atypia and ductal carcinoma in-situ changes (75%). Similarly, IDC grade 2 which formed 59% of all the histological type showed 34 cases (57.6%) with columnar cell change,16 cases (27.1%) with columnar cell hyperplasia, 44 (74.57%) of them showing flat epithelial atypia and 37 (62.7%) of them showing ductal carcinoma in-situ. Only 20 cases of grade 3 carcinoma were there. Among them 6 of them showed columnar cell change, 5 cases showed columnar cell hyperplasia, flat epithelial atypia was seen in 9 cases and 8 cases showed in-situ component.

None of the mucinous and papillary carcinomas of our study showed columnar cell lesions. Only one case of invasive lobular carcinoma was seen which also did not show similar lesions.

Tumour	CCC	CCH	FEA	DCIS
IDC grade I (12)	8(66.6%)	4 (33.3%)	9 (75%)	9 (75%)
IDC grade 2 (59)	34 (57.6%)	16 (27.1%)	44 (74.57%)	37 (62.7%)
IDC grade 3 (20)	6 (30%)	5 (25%)	9 (45%)	8 (40%)
Invasive lobular(1)	-	-	-	-
Mixed(1)	1 (100%)	-	1 (100%)	1 (100%)
Metaplastic (2)	1(50%)	1 (50%)	1 (50%)	1 (50%)
Mucinous (3)	-	-	-	-
Papillary (2)	-	-	-	-
TotaL(IOO)	50%	26%	64%	56%

Table-1: Distribution of columnar cell lesions and carcinoma in-situ in various histomorphological types of carcinoma breast.

FEA		IDC grade			Total	P value
	Others	1	2	3		
Absent	7	3	15	11	36	0.008
Present	2	9	44	9	64	
Total	9	12	59	20	100	

Table-2: FEA and association with carcinoma

DCIS		IDC grade			Total	P value
	Others	1	2	3		
Absent	8	3	22	12	45	0.007
Present	1	9	37	8	55	
Total	9	12	59	20	100	

Table-3: DCIS and association with carcinoma

CCC		IDC grade			Total	P value
	Others	1	2	3		
Absent	7	4	25	14	49	0.016
Present	2	8	34	6	51	
Total	9	12	59	20	100	

Table-4 Columnar cell change and association with carcinoma

CCH		IDC grade			Total	P value
	Others	1	2	3		
Absent	8	8	43	15	72	0.476
Present	1	4	16	5	28	
Total	9	12	59	20	100	

Table-5: Columnar cell hyperplasia and association with carcinoma

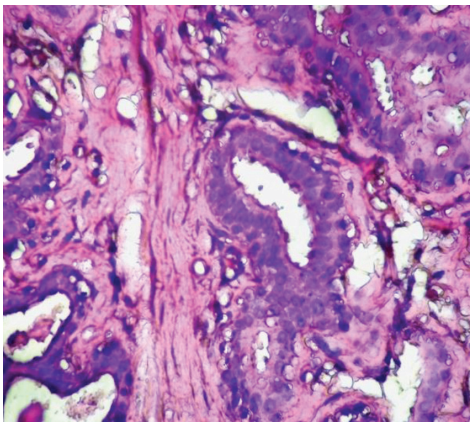

Figure-1: Columnar cell change

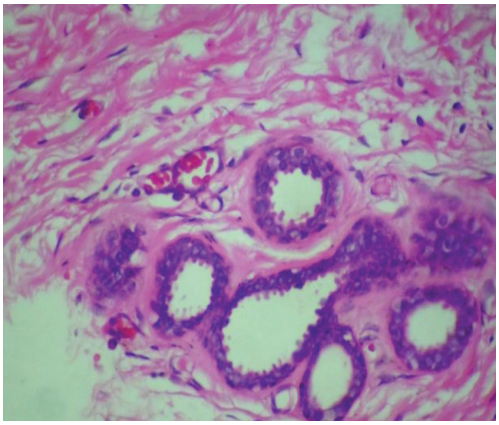

Figure-2: Flat epithelial atypia

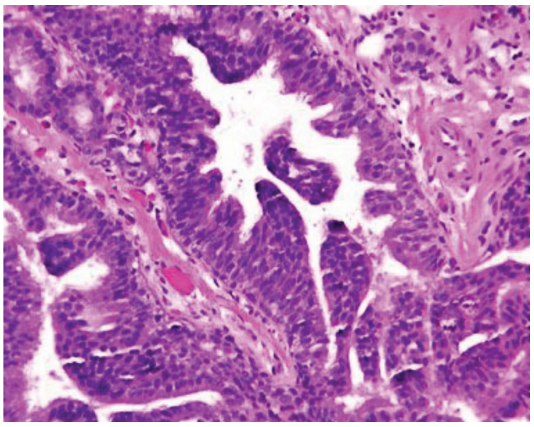

Figure-3: Columnar cell hyperplasia

Simultaneous occurrence of all the three columnar cell lesions was studied. It showed that only 3 cases of the total 12 grade 1 carcinoma, 18 cases of grade 2 carcinomas and one out of the 20 grade 3 carcinomas had all the three lesions together.

Coexistence of flat epithelial atypia and ductal carcinoma in-situ were seen in 66.6% of grade 1 IDC,54% of grade 2 carcinomas and 20% of grade 3 IDC.

Only one male breast carcinoma was there in our study which was a metaplastic carcinoma. But neither of the columnar cell changes could be seen in the adjacent breast tissues sampled.

One or the other columnar cell changes were seen in the majority of invasive ductal carcinomas. All the grade 1 carcinomas of our study showed these lesions either occurring singly as columnar cell change or along with atypia.9 cases of grade 2 carcinomas (15.25%) did not show either of these lesions. Similarly, 35% of grade 31 DC's didn't show any of the columnar cell changes.

So out of the total 100 cases of various types of breast carcinoma we studied, only 23% of them were those who did not show any of the columnar cell changes. This study finally showed that a significant association exists between columnar cell lesions and invasive ductal carcinoma.

DISCUSSION

Adjacent breast tissues were sampled from the mastectomy specimens. Typing and grading of the carcinomas were done. In a published series by Elston c, et al. the most common type of breast carcinoma were those of invasive duct carcinoma NOS which comprised about 40-75%. Our study also had invasive duct carcinoma as the significant bulk (91%).[6]

Presence of columnar cell lesions in different types of carcinoma breast was studied in detail. Columnar cell lesions of the breast can be broadly classified as columnar cell change, columnar cell hyperplasia and flat epithelial atypia. CCC is the simplest form of CCL and is characterized by enlarged TDLUs with variably dilated acini that may have an irregular contour. CCC consists of one to two layers of columnar epithelial cells that have uniform ovoid nuclei oriented perpendicular to the basement membrane and that have no conspicuous nucleoli. Apical cytoplasmic blebs, or snouts, are often present at the luminal surface of the cells, and flocculent secretions may be present in the lumina of the acini. CCH is characterized by enlarged TDLUs with variably dilated acini that may have an irregular contour and are lined by columnar epithelium. However, CCH is characterized by stratification of more than two layers of columnar cells, which sometimes form tufts or mounds with exaggerated apical snouts. Abundant luminal secretions are present, as are microcalcifications. FEA is characterized by enlarged TDLUs with variably dilated acini that are rounded and basophilic. It consists of one or more layers of cuboidal to columnar epithelial cells with cytologic atypia and with apical snouts that may be exaggerated. The chromatin in the nuclei shows clumping and margination, variably prominent nucleoli, and a markedly increased nucleus-cytoplasm ratio. Consequently, the TDLUs have a more basophilic appearance than do those in non-atypical CCLs. The columnar epithelium in FEA may form small mounds, tufts, or short micropapillations; however, complex architectural patterns with rigid cellular bridges are absent.

Our study aimed to search for such lesions in already diagnosed carcinoma breast. Of the total 100 cases which we studied, columnar cell lesions were seen in ductal carcinomas and lobular. Even though we couldn't find all the three lesions together, at least one of these lesions was present in the majority of the cases (66.6% of Grade I carcinoma showed columnar cell change and 75% showed flat epithelial atypia). These observations were in concurrence with the

study by Goldstein et al.[7]

Grade II Carcinomas also showed columnar cell changes in 57.6% cases, flat epithelial atypia in 74.57% and columnar cell hyperplasia in 27.1%.

Another significant finding from our study was the coexistence of FEA and DCIS in 66.6% of grade 1 carcinomas and in 54% of grade 2 invasive ductal carcinomas which is in agreement with the study done by Goldenstein et al.[7] This study also suggests the potential of these lesions to undergo a malignant change in due course.

All the diagnosed cases of grade 1 invasive carcinomas showed the presence of columnar cell lesions either as CCC, CCH, or FEA.

So far many studies have proven that columnar cell lesions, DCIS and invasive carcinomas share similar immunohistochemical profiles. Breast cancer progression is characterized by molecular clonal proliferation.[8,9]

The study done by David JD et al.[10] shows that mutational percentage increased from CCC to invasive ductal carcinoma. The early detection of such lesions in core biopsies will help in preventing the development of invasive carcinomas in the later period. Diagnosis andmanagement of carcinoma breast is by a multidisciplinary team approach. Hence finding of columnar cell lesions without atypia in core biopsies or lumpectomy specimens should alert the clinician to keep the patient under strict follow up with the mammogram.

FEA has got a high percentage risk of progression to invasive carcinoma compared to those without atypia. So if FEA is found in core biopsies, subsequent excision is recommended with wide margins; These margins of excision has to be studied for columnar cell changes. Similarly, if FEA is seen in lumpectomy specimens, especially in the margins, the coexistence of DCIS and ADH component should be looked for and thorough sampling has to be done. Wide excision or mastectomy is recommended in such patients depending upon the age and other factors like the presence of family history.

According to Mascarel et al[11], there is a risk of recurrence of carcinoma in patients whose initial biopsy showed FEA, but the percentage is low. So we can conclude that even in mastectomy specimens if such lesions are detected especially FEA in adjacent breast tissue, there is a minute risk of recurrence of malignancy. So along with chemotherapy, periodic follow-up, motivating the patient for doing regular self-examination of breast and need for ultrasonography/ mammography is emphasized.

CONCLUSION

From our study, we conclude that a consistent correlation exists between columnar cell lesions and Carcinoma Breast which is evidenced by the presence of such lesions in diagnosed cases of carcinoma.

As the tumour bulk is formed by Invasive Ductal Carcinoma, most of the columnar cell lesions were seen in this group. Mostly the lesions were seen in low-grade tumours than in high-grade tumours.

Since columnar cell lesions represent a significant precursor for carcinoma breast, a multidisciplinary modality of approach will help to detect these lesions much earlier and will prove worthwhile. Henceforth the malignancy can be diagnosed at an early stage avoiding the morbidity and mortality of late detection of the disease.

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