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ORIGINAL ARTICLE / RESEARCH

Columnar Cell Lesions of the Breast – Significant or Not?

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ABSTRACT

Columnar cell lesions (CCLs) of the breast range from the innocuous CAPSS (columnar alteration with prominent apical snouts and secretions) to DCIS. Their precancerous potential poses diagnostic and therapeutic riddles, especially in those which show mammographic microcalcifications.

Aims:

1. To document the prevalence of CCLs in the breast.
2. To study their morphologic spectrum.
3. To study the significance of their association with benign and malignant breast lesions.

Material and Methods: One hundred consecutive breast specimens were studied. These specimens included biopsies, lumpectomies and mastectomies. CCLs were classified as per Schnitt criteria. Associated lesions in the adjacent tissue were studied.

Results: Of the 100 samples (43 malignant and 57 benign), 37 cases showed CCL: CAPSS - 23, columnar cell hyperplasia - 11 and columnar cell hyperplasia with atypia - three. The commonest associated lesion was fibrocystic change (n = 54). Their incidence in benign and malignant lesions was 42% and 30%, respectively, with no statistical significance in the difference. Lesions with atypia were seen only in malignant cases.

Conclusions: CCLs are common and often overlooked. These lesions are seen in association with both benign and malignant breast lesions. It is only the presence of atypia in CCL that warrants a special mention and necessitates follow-up, and resection if indicated.

Key words: Columnar cell lesions, breast, CAPSS

Introduction

Columnar cell lesions (CCLs) of the breast are proliferative lesions, commonly encountered in breast biopsies of both benign and malignant breast lesions, especially in those done for mammographically detected microcalcifications. These lesions were also termed previously as blunt duct adenosis, pre-tubular hyperplasia, clinging intraductal carcinoma [1] and flat epithelial atypia.

Some authors have also called it cancerisation of small ectatic ducts by ductal carcinoma in situ cells [2].

CCLs encompass a wide spectrum of morphological patterns, all of which involve the mammary terminal duct lobular unit (TDLU). At one end of the spectrum, there are columnar epithelial cells with terminal snouts lining dilated TDLUs, showing little or no cytoarchitectural atypia, and at other end those that show sufficient cytological and architectural atypia to warrant a diagnosis of atypical ductal hyperplasia [3]. Diagnostic difficulties are encountered at both the

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ends of the spectrum. Schnitt recently classified them as columnar cell change/columnar alteration with prominent apical snouts and secretions (CAPSS), columnar cell change with atypia, columnar cell hyperplasia, and columnar cell hyperplasia with atypia [3]. Those lesions with atypia are said to have a premalignant potential, being a precursor of low-grade ductal carcinoma in situ (DCIS) or invasive carcinoma, more so the tubular type [2].

With this background and a paucity of Indian literature on this entity, we undertook this study on CCLs of the breast.

Aims

The aims of our study were

1. to document the prevalence of CCLs in the breast;
2. to study their morphologic spectrum; and
3. to study the significance of their association with benign and malignant breast lesions.

Material and Methods

- One hundred consecutive breast specimens were studied from June 2003 to July 2005.
- These specimens included biopsies, lumpectomies and mastectomies.
- Exclusion criteria: inflammatory lesions, fibroadenomas and phyllodes tumours were not included, as they had little adjacent breast tissue for study.
- CCLs were classified as per Schnitt criteria and compared with the original descriptions and illustrations provided.
- Associated lesions in the adjacent tissue were studied.
- Fischer's exact test was applied to determine the significance of association with benign and malignant lesions.

Results

Of the 100 breast specimens, 37 showed presence of CCLs. CAPSS was noted in 23 cases, columnar cell hyperplasia in 11 cases and columnar cell hyperplasia with atypia in three cases. The

commonest associated lesion was fibrocystic change ($n = 54$). The list of other associated lesions is given in [Table/Fig 1].

Table/Fig 1

Associated lesion	Total cases
DCIS	4
DCIS and papilloma	1
Epithelial hyperplasia(EH)	1
Fibrocystic change(FCC)	44
FCC-EH	10
Infiltrating ductal Ca	23
Infiltrating lobular Ca	1
Mixed ductal and lobular Ca	3
Mucinous carcinoma	1
No residual tumour – mastectomy specimen	9
Papilloma	2
Paget's disease	1

Associated lesions in the adjacent breast in CCL

Their incidence in benign and malignant lesions was 42% and 30%, respectively. The p value was 0.339, indicating that the difference in association between benign and malignant lesions was not statistically significant (refer [Table/Fig 2]).

Table/Fig 2

	Total number of cases	CCL
Benign	57	24
Malignant	43	13

Association of CCL with benign and malignant lesions

Out of the 23 cases of CAPSS, 10 cases were associated with fibrocystic change, while one was seen with a duct carcinoma.

Of the 11 cases with CCH, the associated disease was fibrocystic change in six cases. Architectural complexity was evidenced by micropapillae in four cases, tufting in five cases, and microcalcifications in one case.

In all the three cases of columnar cell hyperplasia with atypia, the associated disease was malignant.

In two cases, it was an infiltrating ductal carcinoma and in one case, it was high-grade DCIS.

The cytoarchitectural features of the CCLs are detailed in [Table/Fig 3].

	Table/Fig 3			
	Dilated ducts	Micropapillae	Tufting	Calcification
CAPSS	21	0	0	0
CCH	11	4	5	1
CCH with atypia	3	0	0	0

Cytoarchitectural features of CCL

Discussion

CCLs of the breast, as stated earlier, encompass a wide range of morphologic alterations, ranging from the innocuous CAPSS to atypical hyperplasia and DCIS. With an increasing number of breast biopsies being performed for mammographically detected abnormalities, these lesions assume importance, on account of their premalignant potential. We found an incidence of 37% in the current study, implying that they are common in the Indian setting.

Histologically, they comprise of dilated TDLUs, lined by columnar epithelium with a deep eosinophilic cytoplasm and prominent apical snouts [3]. The nuclei are elongated, ovoid and placed perpendicular to the base. The flat lesions without atypia could easily be misinterpreted as apocrine change at low magnification [4]. Careful observation will reveal that apocrine change is characterised by lining epithelium, which contains more abundant granular eosinophilic cytoplasm, a round flattened nucleus with a prominent nucleolus. It is important to make this distinction, as, at times, even flat lesions of CAPSS may harbour cytologic atypia. As one proceeds up the spectrum, cytoarchitectural complexity unfolds, as evidenced by tufting of the lining epithelium, complex micropapillae and foci of microcalcifications. Variable degrees of nuclear atypia are also encountered, sometimes severe enough to warrant a diagnosis of DCIS.

The immunohistochemical profile of CCL shows consistent positivity for oestrogen receptor (ER),

progesterone receptor (PgR), cytokeratin (CK) 19, E-cadherin and negativity for Her2/neu, CK5/6, CK14 and p53. In this respect, CCLs closely resemble ADH and low-grade DCIS as clonal neoplastic proliferations. All categories of CCL exhibit a range of gross chromosomal copy number gains and losses. The genetic hallmarks of well-differentiated DCIS and low-grade invasive carcinomas were observed in CCLs, namely low numbers of chromosomal alterations, more frequent detection of genomic losses relative to gains and the recurrent loss of 16q [5]. These data imply that CCL is a distinct entity both morphologically and pathogenetically. As a lesion, it is still in its infancy, with respect to biological evolution and behaviour, and it is necessary to have large-scale studies to establish the significance of current concepts.

While we did not find significance in association between benign and malignant lesions, what is noteworthy is the fact that the cytoarchitectural complexity and atypia, which were seen in three cases, were all associated with malignancy. When such findings are encountered in breast biopsies done for mammographically suspicious lesions, it is a warning bell. The cores need to be thoroughly evaluated with multiple step sections to exclude malignancy. In excisions, additional tissue needs to be sampled extensively for the same purpose [3].

In conclusion, we would like to emphasise that CCLs of the breast are commonly encountered in our population. When associated with atypia, they need meticulous evaluation to exclude malignancy. Especially, in this era of screen-detected abnormalities, this assumes great significance for both the surgeon and the pathologist. Awareness of this recently characterised entity and its biological implications would go a long way in picking up early cancers and contribute to reducing morbidity.

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