Columnar cell lesions of the breast: radiological features and histological correlation

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Abstract

Objective: This study aimed at investigating the characteristic imaging findings of the columnar cell lesions (CCLs) of the breast via mammography (MG), ultrasonography (US), and magnetic resonance imaging (MRI). **Materials and methods:** The MG, US and MRI findings of 72 patients with histopathological diagnosis of CCLs were retrospectively evaluated. Histopathologically, the CCLs were divided into those with and without atypia; the radiological findings of these two groups were compared with a Chi-square test. **Results:** Sixty-nine patients underwent stereotaxic biopsy (MG-guided in 50 patients and US-guided in 19 patients) and 3 patients underwent US-guided core needle biopsy; all of these patients were diagnosed with CCLs based on a histological examination. The evaluation of the CCLs in patients that underwent MG-guided stereotaxic biopsy revealed that the most common type of microcalcifications were amorphous-indistinct (52%, n= 26/50) and the most common microcalcification distribution pattern was clustered type (76%, n= 38/50). The ratio of CCLs with atypia was similar in patients with high-risk microcalcifications and in those with benign or intermediate-risk microcalcifications (OR: 1.13, 95% CI: 0.573-2.227, p: 0.475). On the other hand, those patients who underwent US-guided biopsies for the evaluation of CCLs had similar proportions of cystic or solid lesions, posterior acoustic shadowing and contour irregularities whether or not they had atypia (p: 0.584, 0.075, 0.187, respectively). Patients with atypia had a higher number of lesions greater than 1 cm via US as compared to those without atypia, but this difference was not statistically significant (p: 0.06). MRI findings were also similar in patients with and without atypia. **Conclusions:** MG revealed that clustered distribution patterns and amorphous-indistinct type microcalcifications were more commonly seen in patients with CCLs; however, there was no significant relationship between US or MRI findings and CCLs. In addition, the MG, US and MRI findings were similar in patients with CCLs that did or did not have histopathological characteristics of atypia.

Keywords: breast, columnar cell lesion, microcalcification, mammography, magnetic resonance imaging, ultrasonography

Introduction

Columnar cell lesions (CCLs) of the breast represent changes in epithelial cells characterized by enlarged terminal ductal lobular units that contain snout cells [1]. CCLs have been described by a variety of terms, including columnar cell change or columnar cell hyperplasia with or without atypia, columnar metaplasia, columnar

alteration of lobules, blunt duct adenosis, columnar alteration with prominent snouts and secretions, enlarged lobular units with columnar alterations, hyperplastic unfolded lobules and hyperplastic enlarged lobular units [2,3]. The World Health Organization Working Group on the Pathology and Genetics of Tumors of the Breast recommended the term flat epithelial atypia (FEA) for CCLs containing atypia. It is important to distinguish CCLs with atypia from those without atypia. The lesions with atypia are often accompanied by ductal carcinoma in situ (DCIS), atypical ductal hyperplasia (ADH) and tubular carcinoma (TC). Therefore, all lesions with atypia must be surgically removed, and every part of the removed specimen should be examined. Recently, advanced digital mammography (MG) techniques have allowed for better detection of microcalcifications. Accordingly, the

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number of biopsies has increased, which has led to the increased detection of CCLs [3]. If specific radiological characteristics of CCLs with atypia can be detected, there may be little need for biopsy in the future.

CCLs are frequently observed via MG as amorphous and fine pleomorphic microcalcifications; this type of microcalcification is also observed in DCIS, ADH, ordinary epithelial hyperplasia, papillomatosis, and sclerosing adenosis [3]. To our knowledge, there is little published regarding the ultrasonography (US) characteristics of CCLs. The two published series we found have a limited number of patients and identified CCLs in lesions with suspicious morphological characteristics via US [4,5].

Further, there are few reports in the literature regarding the imaging characteristics of CCLs, and to our knowledge, no magnetic resonance imaging (MRI) findings of CCLs have been reported in the English literature. Therefore, in the current study, we aimed to identify radiological findings that could indicate CCLs with and without atypia via MG, US and MRI in patients with histopathological proved CCLs.

Materials and methods

The Ethics Committee of the Ankara Oncology Education and Research Hospital approved this retrospective analysis.

Study population and inclusion criteria

Upon review of our hospital database, it was determined that 1570 consecutive needle biopsies under stereotactic MG or US guidance were performed between April 2009 and August 2011.

Patients were included in the study if they had histopathological diagnosis of CCLs and if they underwent MG and US examinations prior to biopsy. Patients were excluded from the study if their histological examination revealed CCLs accompanied by lobular neoplasia (LN), DCIS or TC.

CCLs of the breast were identified in 89 cases (89/1570 [5.6%]). Sixteen lesions were excluded due to their association with concomitant LN (10 patients), DCIS (4 patients) or TC (2 patients). One patient was excluded from the study due to the lack of MG. The remaining 72 patients constituted the study group.

All of the clinical and patient data used in this study were gathered from the electronic medical record system: age, disease symptoms, personal history of breast cancer, number of lesions, lesion size, histopathology results, and imaging results from follow-up. All cases were interpreted by a pathologist with ten years of experience in breast pathology.

Fifty of the 72 patients with histopathologically detected CCLs had suspicious microcalcifications by MG; in these cases, MG-guided wire localization was applied and surgical excision was performed. The other 22 patients underwent US-guided biopsy. In 14 patients from this group US examination showed cystic lesions and fine needle aspiration cytology (FNAC) found suspicious atypia; therefore, US-guided wire localization and excisional biopsy was performed in the second stage and in this way the diagnosis of CCLs was established. In other 8 patients solid lesions were found by US and core needle biopsy (CNB) was performed (5 patients with CCLs with atypia and US-guided excisional biopsy performed during the second phase and 3 patients without atypia in (fig 1).

Fig 1. Algorithm showing patient selection and stages during the diagnosis in patients diagnosed with CCLs (CCLs: columnar cell lesions, DCIS: ductal carcinoma in situ, LN: lobular neoplasia, TN: tubular neoplasia, MG: mammography, US: ultrasonography, CNB: core needle biopsy, FNAC: fine needle aspiration cytology)

The US findings of 50 patients who had indications for excisional biopsy based on the MG findings were retrospectively evaluated. Further, the MG findings of 19 patients with indication for excisional biopsy based on their US findings and 3 patients who underwent only CNB were retrospectively evaluated.

Breast MRI was used for the additional evaluation of inconclusive imaging findings in 10 patients.

Imaging technique

MGs were performed with a dedicated digital MG system (Lorad/Hologic, Danbury, USA). Standard cranio-caudal and mediolateral oblique views were routinely obtained, and further mammographic views were obtained as necessary.

An experienced radiologist performed US with a GE Vivid 3 pro (USA) with 10 MHz linear array transducers.

All of the MRI examinations were performed on a 1.5 MRI System (Signa Horizon Echo Speed; GE Healthcare, Milwaukee, USA) with a bilateral 8-channel breast coil. Standard sequences were obtained as follows: axial T1-weighted spin-echo sequence, sagittal fat suppressed T2-weighted fast spin-echo sequence, axial STIR sequence, and axial T1-weighted 3D fat-suppressed fast spoiled gradient-echo sequence. These sequences were taken prior to and four times after the rapid injection of a bolus of 0.1 mmol/L Gadodiamid (Omniscan, Opakim) per kilogram of body weight followed by 20 ml saline solution.

Two radiologists, one with 10 and one with 5 years of experience in breast imaging, retrospectively reviewed the MG, US and MRI findings; they were in consensus on all findings. The radiologists classified the lesions according to the American College of Radiology Breast Imaging Reporting and Data System (BI-RADS) lexicon [6].

At MG, microcalcifications were classified into four different categories as follows: amorphous or indistinct, fine pleomorphic, coarse and heterogeneous, or round. Their distribution was classified as regional, clustered or segmental. Accompanying findings, such as asymmetric density and architectural distortion, were also noted. If the patient had undergone previous mammographic examinations, the progression of microcalcifications was also observed.

At US, the lesions were classified by their contour, shape, orientation, echo pattern, and internal and posterior acoustic features.

At MRI the shape, margin, enhancement, kinetic curve pattern and T2-weighted appearance of the masses were evaluated.

The histopathology findings were classified as CCLs without atypia or CCLs with atypia.

Statistical analysis

Normally distributed continuous data were expressed as mean $\pm$ SD and categorical data were expressed as n (%). A normal distribution was defined by a histogram and the One Sample Kolmogorov Smirnov Test. The Statistical Package for Social Sciences (SPSS) 13.0 for Windows was used to analyze the data. For continuous variables, a Student's t-test was used to compare differences between groups, and all continuous variables were defined as mean $\pm$ standard deviation (SD). The Chi-square test was used to compare categorical variables, and all categorical variables were defined as numbers and percentages. Linear regression analysis was used to evaluate the association between CCLs with atypia and microcalcification patterns and US findings. A value of $p < 0.05$ was considered statistically significant.

Results

The mean age of the 72 patients was 47.9 ± 6.37 years (range: 34 to 67 years), and 6 of the patients were younger than 40 years. Fifteen patients were admitted with complaints of mastalgia. Palpable painful swelling was observed in 5 patients, while 49 patients were asymptomatic. Two patients had a history of contralateral breast carcinoma.

Histopathologically, 42 lesions were determined as CCLs without atypia (58.3%) and the remaining 30 lesions were associated with atypia (41.6%). The CCLs with atypia were detected in 21 patients that underwent MG-guided biopsy and in 9 patients that underwent US-guided biopsy (Table I).

MG revealed that amorphous-indistinct microcalcifications (52%, 26/50) and fine-pleomorphic microcalcifications (34%, 17/50) were more frequently seen in patients with CCLs (fig 2, fig 3). The most common type of microcalcification distribution pattern was clustered (76%, 38/50). MG also revealed that CCLs with atypia were detected in similar ratios in patients with high-risk microcalcifications and in patients with benign and intermediate-risk microcalcifications (OR: 1.13, 95% CI: 0.573-2.227, $p=0.45$). Moreover, there was no significant difference in the incidence of CCLs with atypia in patients whose MG showed cluster-forming microcalcifications compared with patients that had regional microcalcifications (OR: 1.004 and 95% CI: 0.733-1.376, $p=0.627$).

Further, there was no significant relationship between the CCLs and the US findings. The US findings of the patients who underwent US-guided biopsy are listed in Table II. The greatest dimension of the masses on US ranged from 6 to 20 mm (mean= 10.5 ± 3.8 mm). Comparing the

Table I. Ultrasonography vs mammography findings and histopathological comparison of patients with CCLs.

	Total	CCLs with atypia	CCLs without atypia	P* value
Mammography				
Shape (n, %)				0.45
Round microcalcification	4	3 (75%)	1 (25%)	
Amorphous-indistinct	26	9 (34.6%)	17 (65.4%)	
Heterogeneous	3	1 (33.3%)	2 (66.7%)	
Fine-pleomorphic	17	8 (47.1%)	9 (52.9%)	
Distribution (n, %)				0.62
Regional	12	5 (41.7%)	7 (58.3%)	
Clustered	38	16 (42.1%)	22 (57.9%)	
Accompanying Findings (n, %)				0.31
Asymmetric density	2	0	2 (100%)	
Architectural distortion	1	0	1 (100%)	
Change (n, %)				0.32
Progression	12	3 (25%)	9 (75%)	
Stable	4	1 (25%)	3 (75%)	
Not known	34	17 (50%)	17 (50%)	
Ultrasonography				
Solid lesions (n, %)	8	3 (37.5%)	5 (62.5%)	0.74
Cystic lesions (n, %)				
Simple cyst	1	0	1 (100%)	
Complicated cyst	3	2 (66.7%)	1 (33.3%)	
Complex cyst	10	3 (30%)	7 (70%)	
Posterior acoustic shadowing (n, %)				0.35
Present	6	1 (16.7%)	5 (83.3%)	
Absent	16	7 (43.8%)	9 (56.2%)	
Contour of lesions (n, %)				0.48
Regular	13	5 (38.5%)	8 (61.5%)	
Irregular	3	0 (0%)	3 (100%)	
Indistinct	6	3 (50%)	3 (50%)	
Size of the lesion				0.06
≤1 cm	10	1 (10%)	9 (90%)	
>1cm	12	7 (58.3%)	5 (41.7%)	

P* < 0.05 was statistically significant; CCLs: columnar cell lesions

Fig 2. a. Clustered fine pleomorphic microcalcifications in the upper outer quadrant of the right breast are seen on craniocaudal-mammography, b. Specimen radiography shows that microcalcifications were removed successfully. Pathology detected columnar cell hyperplasia with atypia.

Fig 3. a. Left craniocaudal mammogram shows clustered coarse-heterogeneous microcalcifications in the inner quadrant, b. Specimen radiography demonstrates that microcalcifications were removed successfully. Pathology detected columnar cell alterations.

US findings of patients with CCLs with and without atypia revealed that cystic or solid lesions, posterior acoustic shadowing and contour irregularities were detected in similar proportions in both groups ($p=0.584$, 0.075 , 0.187 , respectively) (fig 4, fig 5). Moreover, the US indication of lesions larger than 1 cm was more common in patients with CCLs with atypia as compared to those without atypia, but this difference was not significant ($p=0.06$).

In 11 patients, MG revealed suspicious microcalcifications; focal ductal ectasia was detected in the localizations of

Table II. The ultrasonographic findings of patients with columnar cell lesions that underwent ultrasonographic-guided biopsy

Solid	8/22 (36.3%)
Cystic	14/22 (63.6%)
• Simple cyst	1 (4.5%)
• Complicated cyst (with low level homogeneous echo)	3 (13.6%)
• Complex cyst	10 (45.4%)
▪ With hyperechogenic debris and thick septations	4 (18.1%)
▪ With irregular thick wall	4 (18.1%)
▪ With solid components	2 (9.09%)

Fig 4. a. The sonogram shows a mass with regular margin, complex echo texture and parallel orientation, b. The mass is seen as hyperintense on the T2 weighted-image (arrow), c. The mass enhancement in the outer quadrant of the left breast on the contrast-enhanced T1-weighted 3D spoiled gradient-echo axial image, d. Kinetic curve assessment of the mass shows a fast initial increase and then a plateau in the post-initial phase. Surgical excision pathology revealed columnar cell changes.

Fig 5. The sonogram depicts a mass with oval shape, lobular contour, complex echo texture, internal hyperechoic component and parallel orientation. Due to the increase in size, surgical excision was performed. Pathology showed columnar cell hyperplasia with atypia.

these suspicious microcalcifications by US. Seven patients had cysts containing thin septa, while 32 patients had no detectable pathology in the localizations of the suspicious microcalcifications. The MG findings of 12 patients who underwent US-guided biopsy revealed dense breast parenchymal structure. Moreover, MG showed nodular densities superimposed with the parenchyma in 8 patients who were determined to have solid lesions based on US. Furthermore, US revealed complex cysts in 2 patients, while MG indicated scattered round and amorphous microcalcifications.

Ten patients underwent MRI after US (6 patients with complex cyst, 2 patients with cyst with irregular thick walls, and 2 patients with regular hypoechoic solid masses on US and family history of breast cancer). There was no significant relationship between the CCLs and the MRI findings, which are described in Table III.

Table III. MRI findings of patients diagnosed with columnar cell lesions

Findings	n (%)
Shape	
Round	9 (90%)
Oval	1 (10%)
Margin	
Regular	6 (60%)
Lobular	4 (40%)
Enhancement	
Peripheric	1 (10%)
Homogeneous	9 (90%)
Kinetic curve	
Plateau	6 (60%)
Wash-out	4 (40%)
T2 weighted	
Hyperintense	9 (90%)
Hypointense	1 (10%)

CCLs: columnar cell lesions

Table IV. The comparison of histopathological findings in patients with columnar cell lesions according to BI-RADs categorization.

BI-RADs	CCLs with atypia	CCLs without atypia
4A	9 (12.5%)	12 (16.6%)
4B	13 (18.05%)	18 (25%)
4C	8 (11.1%)	12 (16.6%)
Total	30 (41.6%)	42 (58.3%)
p*	0.867	

P* < 0,05 was statistically significant, CCLs- columnar cell lesions

BI-RADS 4b category was the most frequently detected in patients with CCLs (43.05%, 31/72). The frequencies of BI-RADS 4a, 4b and 4c were not significantly different in patients with CCLs with and without atypia (p: 0.867) (Table IV).

Discussions

Results of this study show that amorphous-indistinct and cluster-forming microcalcifications were the most frequently seen in the mammograms of patients with CCLs. The radiological findings of patients with CCLs were most frequently associated with the BI-RADS 4b category. No significant difference at US and MG examinations was obtained between the findings of patients with or without CCLs atypia.

Recently, pathological diagnoses of CCLs have increased due to a greater number of stereotactic biopsies performed on suspicious microcalcifications [4]. Therefore the number of studies focusing on CCLs is increasing. Schnitt et al reported that advanced histological imaging and surgical treatment are not necessary in CCLs

without atypia [2]. However, excisional specimens of CCLs with atypia must be examined by removing the sections from all incisions to investigate whether there is accompanying ADH and DCIS [7-9]. Goldstein et al reported that 44% of TCs exist with CCLs with atypia [7], while Leibl et al found that 86% of LN cases were accompanied by CCLs [10]. In the current series, there were 10 (10/89 [11.2%]) CCLs with LN, 4 (4/89, [4.4%]) with DCIS, and 2 (2/89, [%2.2]) with TC. These patients were excluded from the study due to their radiological findings. None of the patients in the current study had concomitant neoplasia.

The most significant problem in the follow-up of benign breast lesions is the risk of developing malignancy. In a series reported by Eusibe et al none of the 25 patients with a confirmed FEA developed invasive carcinoma in 19 years of follow-up [11]. Similarly, Bijker et al reported that none of the 59 patients with benign breast lesions developed invasive carcinoma in 5 years follow-up [12]. These results indicate that there is a very small risk of FEA progressing to invasive cancer. The median follow-up period of the current series was 18 months; none of the 72 patients with CCLs developed local recurrence or invasive breast cancer during that period.

Recently, pathologists have been reporting CCLs after biopsies of suspicious microcalcifications detected by MG. However, the imaging findings and the nomenclature of the CCLs were not investigated in these studies. Kim et al. reported that of 9 lesions from the MG of 9 patients with CCLs, 5 appeared as clustered amorphous-indistinct, 3 appeared as fine pleomorphic and 1 appeared as round microcalcifications [4]. Solorzona et al reported that in the MG of 32 patients with FEA, the most common morphological feature was amorphousness (13/20 [65%]), and the most common distribution was clustered (14/20 [70%]). Other types of microcalcifications reported in Solorzona's study were fine pleomorphic (2/20[10%]) and coarse heterogeneous (5/20[25%]) [5]. In the current study, the most common microcalcification in CCLs was the amorphous-indistinct and clustered type, which is in agreement with the findings of other studies. Additionally, in our study, there were a greater number of fine pleomorphic microcalcifications as compared to the results reported by Solorzona et al. We performed MG-guided biopsies because we observed an increase in the number of round microcalcifications in 4 patients during the follow-up period as compared to the previous year. Patients that had round microcalcifications did not have biopsies during their clinical follow-ups, which might be the reason why less round microcalcifications were detected upon follow-up. In our current study, there was no significant difference in terms of the incidence of high-

risk microcalcifications between patients with CCLs with and without atypia. To our knowledge, there are no studies in the literature comparing the radiologic findings of patients with CCLs with and without atypia.

Upon a review of the literature, we found only two reports of US appearances of CCLs [4,5]. Solorzón et al reported that 9 masses were found in 11 patients (82%), and architectural distortion in 2 patients (18%). Most of the masses displayed an irregular shape (6/9 [67%]) with microlobulated margins (5/9 [56%]) and a hypoechoic or complex echo texture (7/9 [78%]) [5]. Kim et al reported in 12 lesions found in 9 patients non-circumscribed masses in 6 lesions, microcalcifications 4 lesions (3 of microcalcifications were simultaneous with masses) and no US focal lesions in another 5 patients [4]. In the current study, irregular margin and irregular shape were seen in 3% of the lesions, while posterior acoustic shadowing was observed in 6 of the patients who underwent US-guided biopsy (27.6%). However, these malignancy criteria were not reported in the studies by Solorzón et al and Kim et al studies [5,6]. Unlike the literature, we observed a simple cyst at US in one patient with CCLs. FNAC was performed in this patient because the cyst was painful and it increased in size; surgical excisional biopsy was performed because the cytology results indicated the presence of suspicious atypia. In our current study, the US findings of patients with CCLs with and without atypia were similar. However, we might not have seen a significant difference due to the small number of patients in our study.

MRI findings of CCLs have not previously been reported in the English published literature, only a few reports regarding the MRI findings of benign lesions. Sohns et al reported that a plateau of the kinetic curve was seen in 44.2% of cases (42/95 patients), washout was documented in 5.2% of cases (5 patients) and a further increase was seen in 9.4% (9 patients) of cases. Thirty-seven of the benign tumors (38.9%) had a hyperintense appearance on T2-weighted images. Eleven of the 14 (78.6%) oval-shaped tumors had a benign histology, and 14 of the 25 (56%) lobulated tumors were categorized as benign [13]. In the current study, no further increase in the kinetic curve was observed. Only one case had a hypointense appearance on T2-weighted images and most cases had regular and regularly lobular contours. These findings suggest that CCLs show benign features with respect to margin, shape characteristics and their appearance on T2-weighted images. Nevertheless, kinetic curve features can be suspicious and misleading. In addition, MRI can be a confusing method for assessing CCLs since kinetic curve patterns can show plateau or washout. If the radiologist finds a regular mass that is hyperintense on T2-weighted

images and there is a Type 2 or Type 3 kinetic curve, they should consider CCLs in the differential diagnosis.

There were some limitations to this study. Most importantly, the sample size was small and the data was based on the reviews of a single institution. In addition, we did not compare different radiological modalities in terms of the CCLs findings. Further, we might not have been able to see microcalcifications observed in MG with US due to the low density of microcalcifications and the lack of high-definition in devices that we used for investigation. In addition, a dense breast appearance on MG might have masked the lesions, and therefore, we might not have been able to see the same lesions that we saw in the US. Solorzón et al reported that US did not detect any evidence of lesions in 23.6% of the patients that were determined to have lesions by MG [5]. Moreover, Kim et al did not detect any lesions by US in 55.5% of patients that were determined to have microcalcifications by MG [4].

Due to the limited number of patients in our current study, there were no significant differences regarding the US and MR findings of CCLs. While MG showed that the clustered distribution pattern and amorphous-indistinct and fine-pleomorphic microcalcifications were more common in patients with CCLs, there was no significant difference between CCLs with and without atypia in terms of MG findings. The majority of the patients with CCLs were consistent with the BI-RADS 4b category, but the ratios of CCLs with and without atypia were similar with regards to the BI-RADS categories. Our data indicate that there was no difference in the radiological findings of patients with CCLs with and without atypia; in such cases, the differential diagnosis should be made by histopathological examination.

Conclusion

Amorphous-indistinct type and clustered distribution pattern microcalcifications are more commonly seen in CCLs. However, CCLs with and without atypia exhibited similar radiological findings. Further studies with more patients are required.

Conflict of interest: none

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