

Ultrasonography Findings of Breast Microcalcifications without Accompanying Mass and Evaluation of Ultrasound-Guided Biopsy Results

Gamze Durhan ^{1,*}, [MD]

ORCID: 0000-0002-6281-9287

Ömer Önder¹, [MD]

ORCID: 0000-0001-8701-5974

Aynur Azizova¹, [MD]

ORCID: 0000-0002-9354-2612

Jale Karakaya², [PhD]

ORCID: 0000-0002-7222-7875

Kemal Kösemehmetoğlu³, [MD]

ORCID: 0000-0002-7747-0460

Meltem Gülsün Akpınar¹, [MD]

ORCID: 0000-0003-1578-5624

Figen Demirkazık¹, [MD]

ORCID: 0000-0002-4792-840X

¹Department of Radiology, Hacettepe University Faculty of Medicine, Ankara, Turkey

²Department of Biostatistics, Hacettepe University Faculty of Medicine, Ankara, Turkey

³Department of Pathology, Hacettepe University Faculty of Medicine, Ankara, Turkey

Corresponding Author: Gamze Durhan
Department of Radiology, Hacettepe University Medical School, Sıhhiye, Ankara, TURKEY 06410
Tel: +90 5056290664, Fax: +90 3123112145
E-mail: gamzedurhan@gmail.com
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ABSTRACT

Objective: Ultrasonography guided core needle biopsy is a real-time, inexpensive method with higher patient comfort. The aim of this study was to evaluate ultrasonography findings of microcalcifications without accompanying mass and also to investigate the accuracy of ultrasonography guided core needle biopsy results.

Materials and Methods: The study included a total of 54 patients, with microcalcifications observed on mammography and no accompanying mass, who underwent ultrasonography guided core needle biopsy and surgical excision. Core needle biopsy specimen x-rays were obtained from 23 patients. In 11 patients, the location of microcalcification was confirmed by mammography following the administration of contrast agent under ultrasonography guidance. Ultrasonography findings of microcalcifications were identified. The results of ultrasonography guided core needle biopsy were compared with the excisional pathology results.

Results: The microcalcifications without accompanying mass were presented with punctate echogenous foci, hypoechoic area, small distortion, ductal abnormality or fibrocystic changes on ultrasonography. Hypoechoic area and distortion were seen more in malignant lesions, and fibrocystic changes and ductal abnormalities in benign lesions but the difference was not statistically significant. The agreement between ultrasonography guided core needle biopsy and the excisional pathology results was high (Kappa = 0.781). When a specimen x-ray was obtained or core needle biopsy was performed after confirming the location of the microcalcifications with the use of contrast agent, Kappa values were even higher (0.87 and 1, respectively).

Conclusions: Microcalcifications can be seen with targeted ultrasonography imaging and ultrasonography guided core needle biopsy has high accuracy. Obtaining a specimen x-ray, or the use of a trace amount of contrast agent for confirming the location of microcalcifications can increase the accuracy of US guided-CNB.

Keywords: Breast, Ultrasonography, Microcalcifications, Biopsy

INTRODUCTION

Breast microcalcifications are frequently encountered due to the widespread use of mammography as a screening method. Pleomorphic or fine linear branching microcalcifications observed on mammography are most likely a sign of cancer. On the other hand, amorphous or coarse heterogeneous microcalcifications may appear as a finding of early breast cancer or benign disease [1, 2]. If there is a

mass together with microcalcifications, histopathological diagnosis can be made easily with core needle biopsy (CNB) under ultrasonography (US) guidance. However, the diagnosis in these patients may be of a more invasive carcinoma and at a more advanced stage. Microcalcifications observed on mammography without accompanying a mass are generally at the stage of ductal carcinoma in situ

(DCIS) [3]. Although these patients are usually at an earlier stage, histopathological diagnosis is more difficult as there is no accompanying mass on US, and diagnosis is usually made with stereotactic vacuum biopsy or with surgical excision after mammography-guided wire insertion [4, 5]. Excision after mammography-guided wire insertion is a surgical procedure, and in the time until the patient is admitted to the operating room, there may be a change in the location of the wire placed. In addition, patient comfort can be low as a result of sitting position during the procedure and insufficient local anesthesia because of breast compression. Vasovagal syncope can also occur during the procedure. Stereotactic vacuum biopsy can be performed with the patient supine or sitting. High-quality specimens including the calcification can be obtained with this method without the need for any surgical procedure. False-negative rates are low [6], but it is an expensive technique that can only be performed by trained radiology technicians and radiologists. Moreover, in both these methods, the patient is exposed to ionizing radiation.

US remains partially insufficient in the diagnosis of microcalcifications. Characterization of microcalcifications cannot be made with US. However, microcalcifications observed on mammography can be determined on targeted US. Sometimes, ductal changes or a hypoechoic area can accompany microcalcifications [7, 8]. US guided-CNB is an inexpensive, real-time method, with high patient comfort, but it may lead to false-negative results due to small pieces of CNB [8, 9].

The aim of this study was to evaluate US findings of microcalcifications without accompanying mass and also to investigate the accuracy of US guided-CNB results.

MATERIALS and METHODS

Approval for the study was granted by the Ethics Committee of our University.(Approval number: 28.05.2019; GO 19/582; 2019/14-44) As the study was retrospective, informed consent for participation in

the study was not obtained from patients. However, informed consent for the biopsy procedure had been previously obtained from all the patients who underwent biopsy.

Patients

65 female patients who underwent mammography and US guided-CNB between January 2014 and March 2019 were reviewed retrospectively. All these patients were determined with microcalcification not accompanied by a mass observed on mammography, and the microcalcifications were also observed on US.

Male patients and patients with microcalcification accompanied by a mass were not included in the study. In addition, a total of 11 patients were excluded who did not have excisional pathology results or follow-up in our hospital.

Finally, 54 patients were included in the study.

Radiological Imaging

Digital mammography images were obtained by taking 2 views, standard mediolateral oblique and craniocaudal, for each breast using a Seno Essential mammography device (General Electric, USA). For characterization of the microcalcifications, a magnification view was also obtained.

After evaluation of the microcalcifications on mammography, targeted US was applied. The US device used was a Toshiba Aplio 400 with a 12 MHz linear probe (Toshiba Medical Systems Corporation, Otawara, Japan).

Although there was no mass with the microcalcifications, any accompanying small structural distortion, hypoechoic area, ductal and fibrocystic changes were recorded. In 11 patients who had only punctate echogenic foci without accompanying findings, 0.1 cc contrast agent (Iohexol 300 mg/100 ml) was administered with an insulin injector under US guidance and a single mammography image was obtained to be sure about the location of microcalcifications. Following observation of the contrast agent in the same location with the microcalcifications, US guided-CNB was performed (Figure 1).

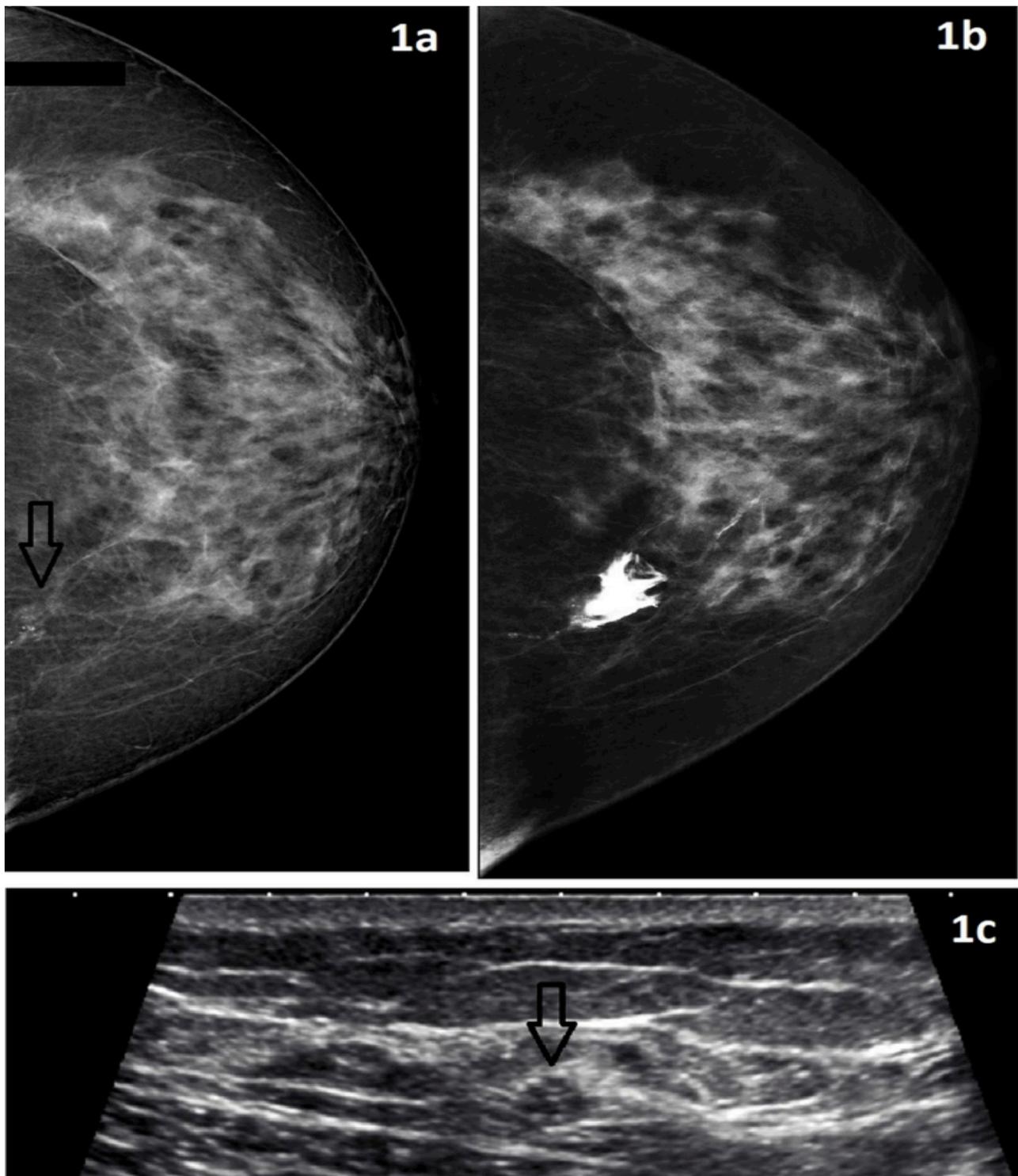


Figure 1. Microcalcifications observed on craniocaudal mammography image (1a). Area suspected of microcalcifications with no accompanying mass observed on US (1 c) Following injection of 0.1 cc contrast agent to the suspected area on US, microcalcifications and contrast agent are seen at the same location on craniocaudal mammography image (1b)

Pathology Evaluation

At least 4 pieces of CNB were taken with a 14G fully automatic needle from microcalcifications that could be localized on US. From 23 patients, specimen x-rays of CNB were obtained and the presence of microcalcifications was identified (Figure 2). Surgical excision

was performed to the patients according to the CNB results and radiological findings. Evaluations were made by comparing the CNB results with the surgical excision results.

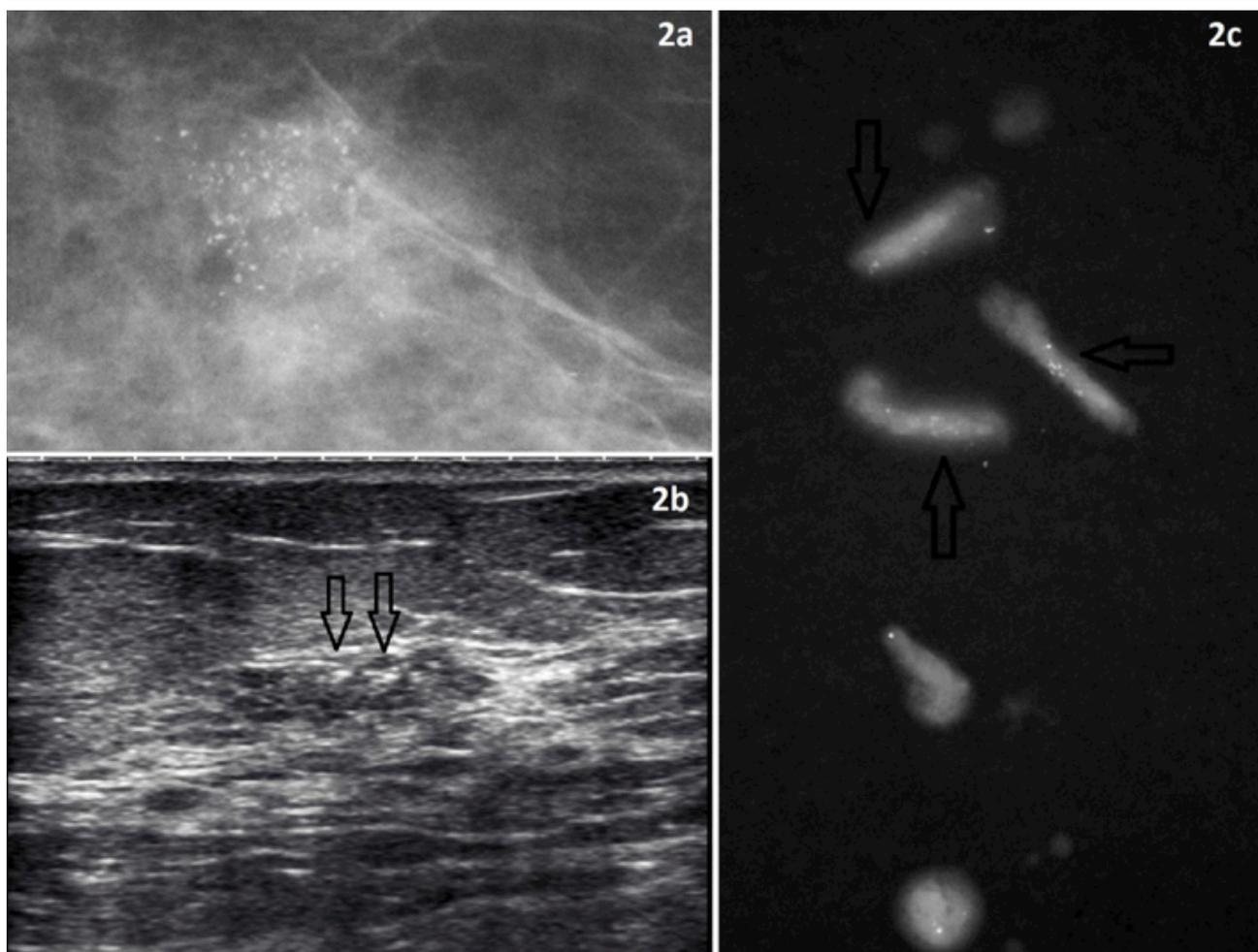


Figure 2. Microcalcifications observed on craniocaudal mammography image (2a). Suspected area observed on US image (2b). Microcalcifications were demonstrated on specimen x-ray of CNB (2c).

Statistical Analysis

Data obtained in the study were analyzed statistically using IBM SPSS 23.0 software. Descriptive statistics were stated as number (n) and percentage (%) for categorical variables and as mean \pm standard deviation values for numerical variables. To examine the agreement of measurements related to the same variable (pre and postoperative pathology results), the Kappa coefficient was calculated. The results of the relationship of two measurements were compared with the McNemar Bowker test. The Chi-square test was applied to examine whether or not there was any relationship between categorical variables. A value of $p < 0.05$ was accepted as statistically significant.

RESULTS

Clinical and Histopathological Findings

The mean age of the patients was 50.7 ± 12 years. The

mean size of the lesions was 32.5 ± 30 mm. Of the total 54 lesions, 12 were benign and 42 were malignant. The pathology results of the 12 benign microcalcifications were reported as 5 ductal epithelial hyperplasia without atypia, 4 fibrocystic changes and 3 sclerosing adenosis.

The 42 malignant microcalcifications were reported as 31 DCIS and 11 invasive ductal carcinoma.

The agreement between the CNB and excisional pathology results was determined to be high (Kappa = 0.781, $p < 0.001$) (Table 1). When the CNB results and excisional pathology results were evaluated in respect of differentiation between only benign and malignant (DCIS and invasive carcinoma), the agreement was higher (Kappa = 0.852, $p < 0.001$).

Table 1. The agreement between the CNB and excisional pathology results

		Excisional Pathology Results			
		Benign (n)	Grade 2 DCIS (n)	Grade 3 DCIS (n)	IDC (n)
Core	Benign	12	1	2	0
	Grade 2 DCIS	0	5	1	0
Needle	Grade 3 DCIS	0	0	22	4
	IDC	0	0	0	7
Biopsy	Total	12	6	25	11
Results					

DCIS: Ductal Carcinoma in situ, IDC: Invasive Ductal Carcinoma, n: number. Kappa = 0.781, $p < 0.001$.

Comparisons of Radiological Findings and Histopathological Findings

The BI-RADS categories of the microcalcifications were BI-RADS 4A:11 lesions, BI-RADS 4B: 16, BI-RADS 4C: 16 and BI-RADS 5: 11. A statistically significant difference was determined between the excisional pathology results according to the BI-RADS category ($p < 0.001$). Of the patients determined as BI-RADS 4A, 72.7% were benign, 18.8% of the BI-RADS 4B lesions and 6.3% of the BI-RADS 4C lesions. None of the BI-RADS 5 lesions were determined with a benign pathology result.

A total of 21 lesions were observed as only

microcalcifications with punctate echogenicities on US. And in 11 patients, US guided CNB was performed after the location was confirmed with the administration of contrast agent. The accuracy of CNB with this method was very high. The excisional pathology results and the CNB results were the same in all these patients (kappa=1).

Accompanying findings of the microcalcification were hypoechoic area (n:16), ductal abnormality (n:7), distortion (n:6) and fibrocystic changes (n:4) (Figure 3).

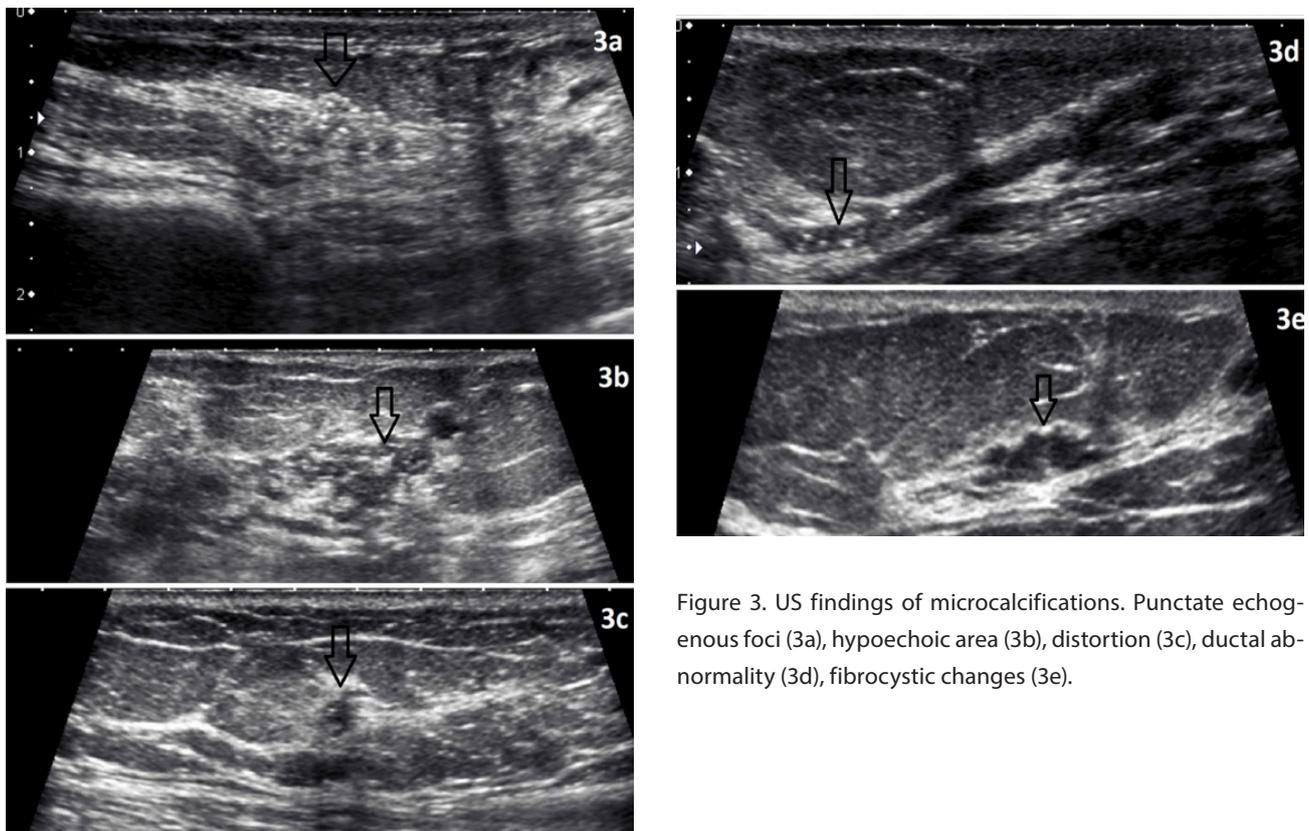


Figure 3. US findings of microcalcifications. Punctate echogenic foci (3a), hypoechoic area (3b), distortion (3c), ductal abnormality (3d), fibrocystic changes (3e).

In patients with grade 3 DCIS and those with invasive carcinoma, hypoechoic area (grade 3 DCIS 32%, invasive carcinoma 45.5%) and distortion (grade 3 DCIS 16%, invasive carcinoma 18.2%) were more common, while in those with benign pathology results, fibrocystic changes (16.7%) and ductal abnormality (25%) were more common. But, it could not reach statistical significance ($p=0.4$).

Radiological and Pathological Evaluation of Specimens

A CNB specimen x-ray was obtained for 23 lesions and the presence of microcalcifications was confirmed. In these patients, the agreement between the CNB and excisional pathology results was high ($Kappa = 0.87, p < 0.001$). Specimen x-ray was not taken for the other 31 patients. Of these, the CNB pathology result was malignant in 24 patients and the presence of microcalcification was not reported in the pathology results as malignancy had already been observed. In 5 patients, the pathology was reported to include microcalcification and all of them were benign. No microcalcification was reported to have been observed in the pathology reports of 2 patients. Although the pathology results of CNB were benign, the final excisional pathology result was reported as malignant.

DISCUSSION

The main findings of this study were first, that just as microcalcifications with no accompanying mass may be observed as punctate echogenic foci on US, they may also be seen in the form of accompanying small structural distortion, hypoechoic area, cysts or ductal abnormalities. Second, the accuracy of US guided-CNB is high, and finally, the agreement with excisional pathology results increased when a specimen x-ray was obtained or when biopsy was performed after confirming the location of microcalcifications with contrast agent.

Microcalcifications have become more commonly seen with the increase in mammography screening. Characterization of the microcalcifications is made according to the morphological features and extent

on the mammography. Coarse heterogeneous and amorphous microcalcifications are observed in malignancies at a lower rate than pleomorphic and fine linear branching microcalcifications [10, 11]. The characterization of microcalcifications is made on the mammography, but on US, microcalcifications can be observed with good spatial resolution and contrast resolution. It is more difficult to observe microcalcifications in echogenous breast tissue on US. However, with newly-developed technologies, calcification algorithms have increased the visualization of microcalcifications on US [12].

As microcalcifications can be seen on US, a biopsy performed under US guidance is a highly advantageous method as it is inexpensive, comfortable, provides real-time imaging and does not involve radiation exposure. Therefore, it is important to detect the corresponding microcalcifications observed on mammography on US. While these are sometimes observed only as punctate echogenous foci in breast tissue, sometimes, as in the current study, they can be seen as accompanying hypoechoic area, fibrocystic changes, small structural distortion, ductal ectasia or ductal abnormalities in the form of irregularities in the ducts [12, 13].

In the current study, while the BI-RADS category could accurately predict the histopathological diagnosis of microcalcifications, no statistically significant result was reached in the US findings. Nevertheless, hypoechoic area and distortion were observed more in malignant lesions and fibrocystic changes and ductal abnormalities were seen more in benign lesions. Previous studies have reported that microcalcifications observed on US have a greater likelihood of being malignant and they have been observed in higher grade DCIS [14, 15]. And this may be the reason for the low number of benign microcalcifications and absence of low-grade DCIS patients in the current study. On the other hand, the detection of a mass accompanying microcalcifications is generally a sign of invasive carcinoma. As patients with an accompanying mass were excluded from the study, few patients were diagnosed with invasive carcinoma.

According to the results of the current study, the

accuracy of US guided-CNB was high (Kappa=0.781). When evaluation was made of the excisional pathology results and the CNB results in respect of differentiation of only benign or malignant (DCIS and invasive carcinoma), the agreement was higher (Kappa =0.852). When CNB specimen x-ray was taken (Kappa = 0.87) or biopsy was performed after the location of microcalcifications was confirmed with contrast agent (Kappa = 1), the agreement with the excisional pathology results increased. When it is considered that in stereotactic vacuum biopsy there is radiation exposure, it is an expensive procedure, and the device is not available everywhere, US guided-CNB can be applied safely.

When there is radiologic-pathologic discordance, the patient may be referred for stereotactic vacuum biopsy under mammography guidance or excision after mammography-guided wire insertion. In the current study, only 3 patients were reported as malignant in the excisional pathology results despite the benign pathology result of CNB. CNB specimen x-ray had not been taken in these patients. No microcalcification was reported to have been observed in the pathology reports of 2 patients. In such cases, as in these current study patients, it is important that microcalcification is not reported in the biopsy material by the pathologist. Various methods have been developed to be able to perform biopsies of microcalcifications under US guidance. One of these is the method described by Lee et al of vacuum biopsy performed after placement of a wire under US guidance [16]. However, the expensive vacuum needle biopsy is again used in this method, and another interventional procedure is performed for placement and removal of the wire. In the current study, the results of the CNB performed after confirming the location of the microcalcifications using a trace amount (0.1cc) of contrast agent were 100% accurate. This method, which has not been commonly

described in literature, can be safely used for confirming the location of microcalcifications under US guidance and for biopsy.

There were some limitations to this study. First was the small size of some patient groups, especially patients with a benign or invasive carcinoma diagnosis. However, invasive carcinoma is generally accompanied by a mass on US, and as patients with an accompanying mass were excluded from this study, this group of patients was small. The low number of patients with benign microcalcifications can be attributed to the difficulty of identifying benign microcalcifications on US and that biopsy in these patients is usually performed under mammography guidance. And also some patients underwent to radiological follow-up instead of surgical excision after the results of benign CNB. Another limitation was that a specimen x-ray was not taken for each patient and the number of patients with confirming of the location of microcalcifications with contrast agent was very low.

CONCLUSION

Microcalcifications with no accompanying mass on mammography can be observed on US in the form of punctate echogenous foci, hypoechoic area, small distortion, ductal abnormality or fibrocystic changes. US guided-CNB can be used in the diagnosis of microcalcifications with high accuracy rates. Obtaining a specimen x-ray, or the use of a trace amount of contrast agent for confirming the location of microcalcifications can increase the accuracy of US guided-CNB.

CONFLICT of INTEREST

The authors declare that they have no conflict of interest.



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