

The Ultrasonic Diagnosis of Nonpalpable DCIS Without Calcification on MMG and Nipple Discharge: Advocacy of a New Term, 3 Non-DCIS

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Summary. Ductal carcinoma in situ (DCIS) has been detected primarily by palpation, calcification on mammogram (MMG), and nipple discharge. Ultrasonographic investigation of DCIS has been performed, but has not up to now revealed any form of DCIS that could not be discovered by the above three methods. In the present report, we describe a form of DCIS that has not been detected by earlier methods, and propose to refer to this new DCIS as 3 non-DCIS to distinguish it from conventional DCIS: 3 non-DCIS represents nonpalpable DCIS without calcification on MMG and without nipple discharge. Only the method of ultrasound screening described in this chapter can detect 3 non-DCIS. We diagnosed 23 patients as 3 non-DCIS at this institution between May 1997 and March 2003. There was neither calcification, mass, nor distortion on MMG in these patients. On ultrasonography, a small mass measuring 10 mm or less was revealed. Thorough examination by fine-needle aspiration cytology showed 90% of the patients were positive. On analysis of subtype of DCIS, 22 of the 23 cases of DCIS were classified into pure noncomedo type and 1 was mixed type. Lesions in 3 non-DCIS were frequently less extensive than those in conventional DCIS.

Key words. Ductal carcinoma in situ, Ultrasonography, Nonpalpable breast cancer, Breast conservation therapy

Introduction

Ductal carcinoma in situ (DCIS) has been detected primarily by palpation, calcification on mammogram (MMG), and nipple discharge. Ultrasonographic investigation of DCIS has been performed but has not up to now revealed any form of DCIS that could not be discovered by these three methods [1, 2]. In the present report, we describe a form of DCIS that has not been detected by earlier methods, and propose to refer to this new DCIS as 3 non-DCIS to distinguish it from the conventional DCIS. Thus, 3 non-DCIS represents nonpalpable DCIS without calcification on MMG and without nipple discharge. Only the method of ultrasound screening described in this report can detect 3 non-DCIS.

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We diagnosed 23 patients as 3 non-DCIS at this institution between May 1997 and March 2003. There was neither calcification, mass, nor distortion on MMG in these patients. On the ultrasonograph, a small mass measuring 10 mm or less was revealed. Thorough examination by fine-needle aspiration cytology showed 90% of the patients were positive. On analysis of subtype of DCIS, 22 of the 23 cases of DCIS were classified into pure noncomedo type and 1 was mixed type. Lesions in 3 non-DCIS were frequently less extensive than those in old DCIS.

The Crux of Detecting 3 Non-DCIS

We performed ultrasonography with a unit of SSD-1000 (Aloka) of annular alley type. To detect 3 non-DCIS, we need to discover a very slight change in the breast on ultrasound whole-breast scanning. It is hard to detect 3 non-DCIS by just looking for a mass. It is important for ultrasonographers to have their attention concentrated on the continuity of internal patterns of the breast structure on the border between the mammary region and adipose tissue, and the duct, mottle, and adipose tissues, to instantly catch any fine break in the continuity of the monitoring images [3].

Findings on Ultrasonography

The ultrasound findings in the 23 cases (Fig. 1) were classified into five groups. (1) Relatively well-defined small masses were detected in 18 cases. The major diameter of the masses was 3–10 mm on ultrasonograph. The lesions were too small to

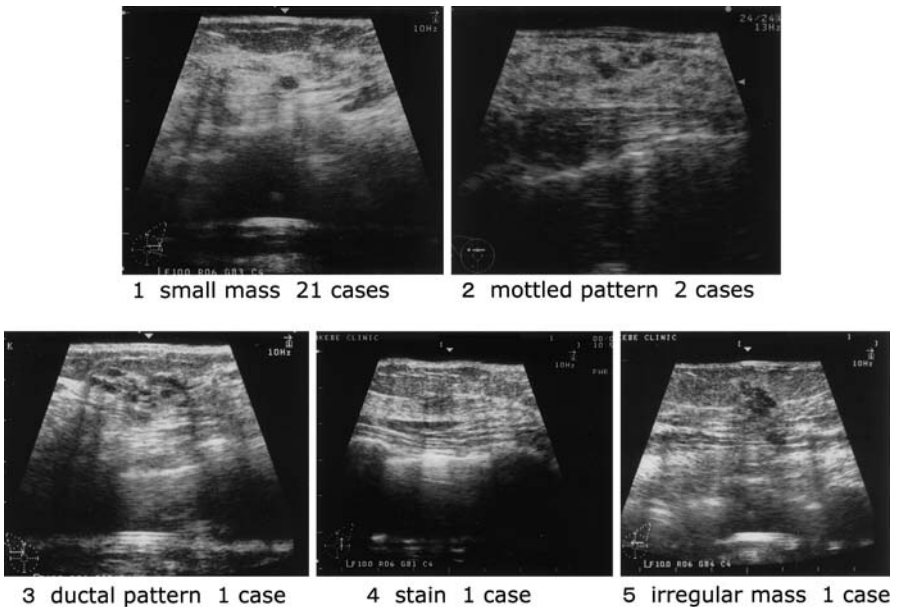


FIG. 1. Ultrasonography (US) findings of 3 non-DCIS

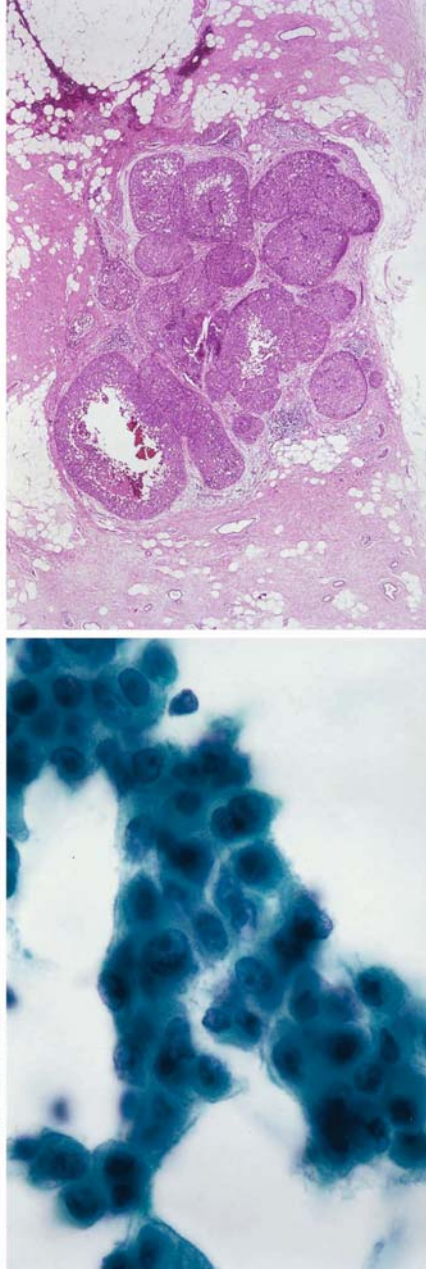
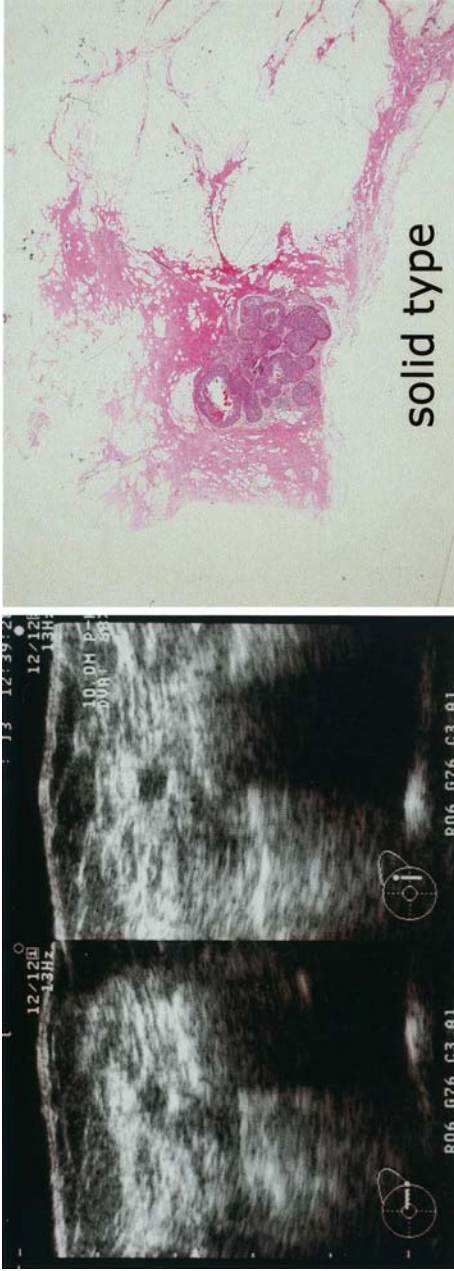


FIG. 1. A 68-year-old woman was found to have a low-echo area measuring 5 mm in the left breast on mass screening. The area was well defined, with a small DW ratio, and the findings appeared to be suggestive of a benign cyst or adenoma. A large amount of slightly atypical cells were obtained by fine-needle aspiration cytology, and class 5 (suspected papillotubular cancer) was diagnosed. Pathologically, the lesion was a localized solid-type ductal carcinoma in situ (DCIS)

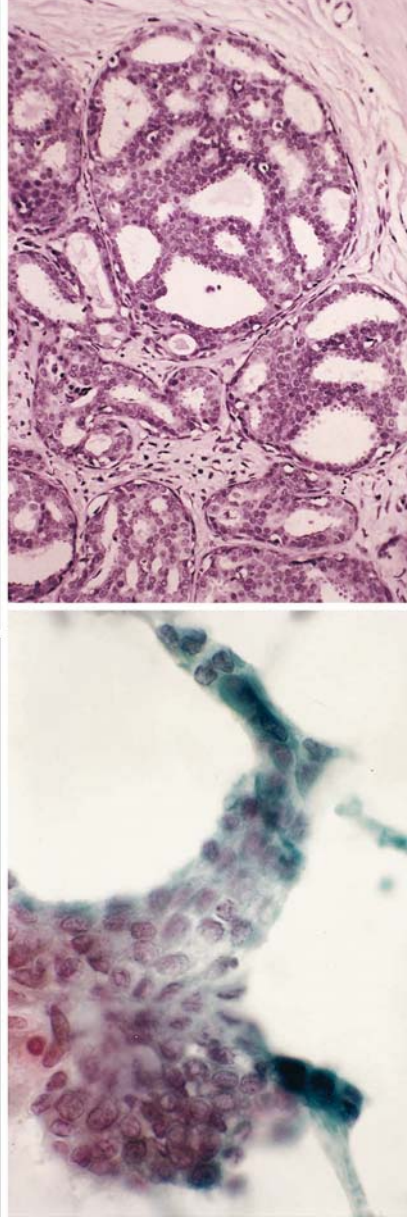
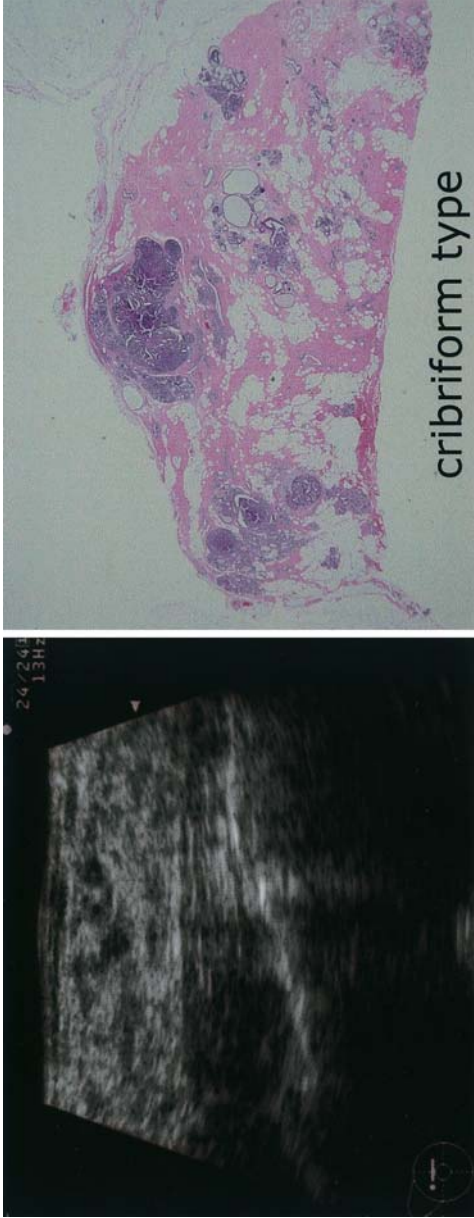


FIG. 3. Case 2. A 46-year-old woman came to the hospital because of premenstrual pain in the breasts. There was an area measuring 10 mm in diameter with slight irregularity in the mottled pattern at the upper region of the right breast. Because fine-needle aspiration cytology yielded a large amount of strongly atypical cells, class 5 (suspected invasive cancer) was diagnosed. Histopathological examination showed a cribriform-type DCIS spread over an area measuring 30 mm

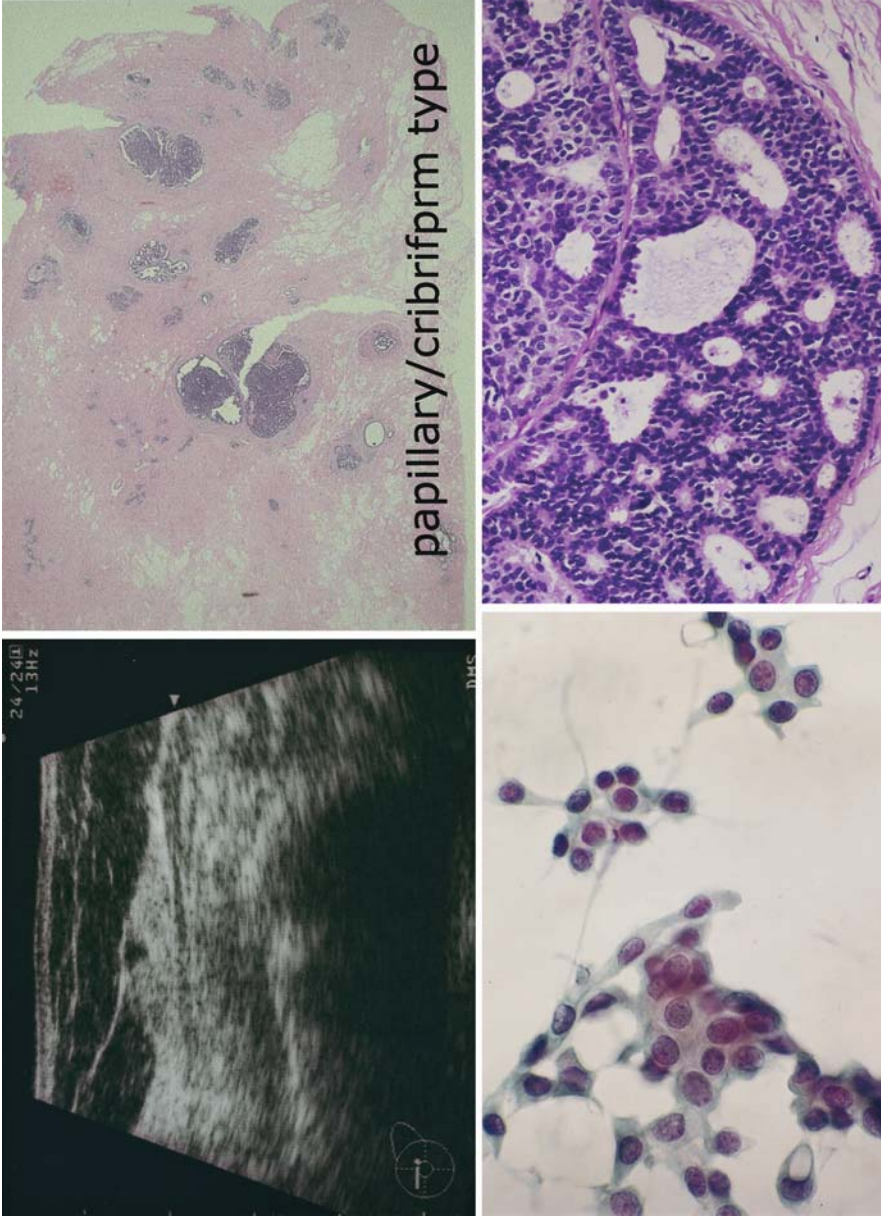


FIG. 4. Case 3. A 67-year-old woman was diagnosed as having a cystic lesion measuring 3 mm at the upper region of the right breast on mass screening. Surrounding it were several smaller low-echo areas in a segment. The diagnosis by cytology was class 4 (suspected DCIS). Histopathological examination revealed a papillary-type DCIS spread over a 50-mm area. In such older patients, especially those who had menopause 10 years or more before, small cystic lesions in the breast frequently seem to be DCIS, and therefore, fine-needle aspiration cytology should be actively performed

evaluate the shape, internal echo, and DW ratio, etc. There was no attenuation in posterior echoes. (2) An irregular mottled pattern within a 10-mm area was detected in 2 cases. (3) A cluster of ducts with a dilated ductal pattern was seen in 1 case. (4) There was a stain, a poorly defined area with lower echoes than those in the surrounding mammary gland tissue; it was termed a “stain” because it seemed like a stain on a shirt that cannot be cleaned by washing. (5) Typical ultrasonographic findings for breast cancer, that is, an irregular mass invading adipose tissue, appeared in 1 case.

Close Examination

Fine-needle aspiration cytology alone was performed, and core-needle biopsy was not used. Core-needle biopsy is too expensive to use in evaluating 3 non-DCIS because needle biopsy at many sites is needed. In addition, we consider that cytology with a fine needle is more convenient in accurately inserting a needle to reach a small lesion measuring only approximately 5 mm. Fine-needle aspiration is performed manually without using an adapter. A 7-cm, 23-gauge needle is inserted at a site on the right side of a scanner under the guidance of ultrasound. Caution should be taken in handling the needle so it does not stick out of the lesion. Considerable amounts of cell specimens were collected by aspiration in all of the 23 cases with 3 non-DCIS. The results of cytology were evaluated as class 5 (suspected invasive cancer) in 3 cases, class 4 (suspected DCIS) in 15 cases, class 3b (suspected DCIS, but papilloma cannot be ruled out) in 2 cases, and class 3a (suspected papilloma) in 2 cases. The sensitivity of cytology was considered 90% if class 3b or more severe classes are considered positive. This finding shows that fine-needle aspiration cytology allows diagnosis without using core-needle biopsy.

Histological Findings

Almost all the histopathological findings in cases of 3 non-DCIS (Table 1) indicated the features of noncomedo type of DCIS. Only 1 case was evaluated as a significant mixed type. Thin slices with the thickness of 5 mm of tissue specimens were examined. Localized lesions were found in 13 cases, lesions measuring 4 cm or less in 9 cases, and extended lesions measuring more than 4 cm in 4 cases. DCIS lesions were smaller in cases of 3 non-DCIS than DCIS with calcification diagnosed in our facility.

TABLE 1. Pathological features of 3 non-DCIS

FNAC	Class IIIa	Class IIIb	Class IV	Class V
	2	2	14	8
Subtype	Pure noncomedo	Comedo mixed	Pure comedo	
	25	1	0	
Spread	No spread	Spread \leq 4 cm	Spread >4 cm	
	13	9	4	

DCIS, ductal carcinoma in situ; FNAC, fine-needle aspiration cytology

TABLE 2. Differential diagnosis of small cystic lesion

	Concentrated cyst?	DCIS?
Age (years)	Less than 40	More than 60
Size	Less than 3 mm, more than 10 mm	3–10 mm
Shape	Regular	Irregular
Spread	Scattered	Solitary or clustered
Internal echo	Homogeneous	Irregular
Posterior echo	Attenuated	Unchanged

Differential Diagnosis

On ultrasonography, a cyst, especially one containing condensed material, is hard to differentiate from 3 non-DCIS. Even a skilled investigator with long experience finds it hard to differentiate the two only by findings on ultrasonography. Differentiation of the two needs the investigation of the following factors. DCIS was frequently detected in older patients (Table 2). The area of concern is likely to be a cyst if posterior echoes attenuate and to be DCIS if posterior echoes do not change. The posterior echo attenuation is the point of differentiation between a cyst and palpable carcinomas. It is impossible to differentiate 3 non-DCIS from papilloma on an ultrasonograph. Screening skill and high diagnostic ability are required for differential diagnosis.

Results of Screening

The results of a mass screening by whole-breast scanning using ultrasonography follow. The greatest proportion of the participants were enrolled in this hospital. The number of participants includes that of repeat participants. Over 6 years, 12 404 persons were examined and 60 were diagnosed as having breast cancer; 29 had nonpalpable breast cancer and 14 had 3 non-DCIS. The detection rate of breast cancer by the above method was 0.48%, which is more than four times the detection rate by macroscopic observation combined with palpation in Japan, and higher than that by mammography. This high detection rate is due to the detection of nonpalpable breast cancers, especially 3 non-DCIS. With skills to diagnose 3 non-DCIS, ultrasonography will be more useful than mammography.

Concept of 3 Non-DCIS

There is a question about DCIS that has remained unresolved for us. Invasive carcinoma is not confined to those cases of carcinoma that show calcification on MMG or which are accompanied by discharge from the nipple. Of all cases of invasive carcinoma, calcification is positive on MMG in about half of all cases, and the percentage of invasive carcinoma accompanied by nipple discharge is lower and estimated to be about 10%. Most invasive carcinoma should first assume the form of DCIS within the breast. Then, why do most of the nonpalpable small DCIS undergo calcification? Why

is their detection precipitated only by discharge from the nipple? There should be many cases of DCIS not accompanied by calcification or nipple discharge. We think 3 non-DCIS represents such cases of DCIS.

In Western countries, the outcome of breast conservative therapy for DCIS shows that lumpectomy alone resulted in recurrence of 15% or more, and lumpectomy combined with radiotherapy resulted in recurrence of 10% or more [4, 5]. Most DCIS is detected on the basis of calcification on MMG in Western countries. Of 15 patients with 3 non-DCIS in whom we performed breast conservative therapy in the previous and present hospitals, all have survived for 5 years, and no recurrence has been noted in these patients. Although no inference can be made from the results of such a small number of cases, localized lesions and noncomedo type of DCIS, as evaluated on histopathological examination, are likely to have contributed to such a low recurrence rate. We consider that breast conservative therapy should be indicated for 3 non-DCIS separately from regular DCIS in each treatment plan.

Conclusion

1. The category 3 non-DCIS is nonpalpable DCIS without calcification on MMG and without nipple discharge.
2. Diagnosing 3 non-DCIS requires excellent ability on the part of the investigator in detecting small lesions on the ultrasonograph, the accurate application of fine-needle aspiration, and experience in diagnosing by cytology.
3. Frequently, 3 non-DCIS is revealed as a well-defined mass on the ultrasonograph. Small cystic lesions (approximately 5 mm) in elderly patients who had menopause 10 years or more before were frequently diagnosed as 3 non-DCIS.
4. In the present cases of 3 non-DCIS, the histopathological type was diagnosed as noncomedo type, which was more localized than DCIS with calcification.

References

1. Ueno E (1996) Recent progress of imaging diagnosis for breast cancer: breast ultrasound and color Doppler. *Jpn J Breast Cancer* 11(2):216–231
2. Kamio T, Kameoka S, Muraki H, et al. (1991) Significance of ductal findings in ultrasonic examination of the breast. Diagnosis of intraductal tumor and intraductal spreading of breast cancer. In: *Topics in breast ultrasound*. Shinohara, Tokyo, pp 200–205
3. Takebe K, Nakamura K, Yamamoto Y (1999) The contribution of ultrasound examination to the diagnosis of nonpalpable breast cancer. *Jpn J Breast Cancer* 14(4):444–450
4. Fisher B, Dignam J, Walmark N, et al. (1998) Lumpectomy and radiation therapy for the treatment of intraductal breast cancer: findings from National Adjuvant Breast and Bowel Project B17. *J Clin Oncol* 16:441–452
5. Julien JP, Bijker N, Fentiman IS (2000) Radiotherapy in breast-conserving treatment for ductal carcinoma in situ: first results of the EORTC randomised phase III trial 10853. *Lancet* 355:528–533