



## Breast Imaging

## Clinical, mammographic, and ultrasonographic characteristics of diabetic mastopathy: A case series

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## ARTICLE INFO

## Keywords:

Diabetic mastopathy  
Mammography  
Ultrasound

## ABSTRACT

**Purpose:** Diabetic mastopathy (DMP) is a rare benign breast lesion that mimics breast cancer on ultrasound. Our aims were to identify patient characteristics and imaging features of the disease.

**Methods:** We conducted retrospective searches of our database for DMP lesions that were pathologically confirmed between January 2004 and November 2015. Mammographic and ultrasound features were reviewed by two experienced radiologists.

**Results:** Twelve women were identified with 16 lesions. Most patients (83%) had type 2 diabetes mellitus (DM) and over half were insulin-dependent (58.3%), with a mean time of 16.9 years between the diagnosis of DM and that of DMP. There were negative findings on mammography for 46.7% of the lesions, including larger-sized lesions. Ultrasound revealed various features, including irregular shape (81.3%), indistinct margins (100%), parallel orientation to the chest wall (93.8%), marked hypoechoogenicity (87.5%), and posterior shadowing (62.5%).

**Conclusions:** DMP was more common in patients with longstanding DM; in particular, type 2 DM and insulin-dependent patients. DMP lesions were usually occult on mammography, despite the relatively large size of DMP, which may help distinguish DMP from invasive cancer. Ultrasound detected several features that are also present in invasive cancer, making tissue sampling necessary to distinguish these.

## 1. Introduction

Diabetic mastopathy (DMP) is a rare fibrotic disease of the breast and comprises < 1% of all benign breast lesions [1,2]. It was first described in 1984 by Soler and Khardori [3] as fibrotic breast lesions in women with longstanding diabetes mellitus (DM), especially in premenopausal women with a prolonged duration of type 1 DM [1,2,4–8]. Later studies [9–11] observed that DMP is also associated with type 2 DM. The majority of cases of DMP patients have diabetic complications such as retinopathy, nephropathy, or neuropathy [12].

DMP often presents as a non-tender palpable mass and it is also detected during mammographic screening of asymptomatic patients. The mammographic features have been reported as nonspecific, whereas the ultrasound features mimic those of breast cancer [2,13,14]. Therefore, the diagnosis of these lesions is usually histological. The pathological features of DMP include keloid-like fibrosis, lymphocytic

lobulitis and ductitis, lymphocytic vasculitis, and the presence of epithelioid fibroblasts. The predominant lymphocytic infiltration in DMP is B-cells; whereas, in lesions other than DMP it is T-cells [4,15–17].

Recognizing the tell-tale patient characteristics and the key imaging features of DMP is crucial for detection of this rare disease to avoid unnecessary surgical excisions that could exacerbate it [1,2,18].

In this study, we sought to determine the patient characteristics and the mammographic and ultrasound features of DMP to distinguish from the invasive cancer.

## 2. Materials and methods

This study was approved by our hospital's institutional review board for human investigation. The database of pathology reports at our hospital (Thanyarak Breast Center, Siriraj Hospital, Mahidol University, Thailand) was searched between January 2004 and November 2015

**Abbreviations:** BI-RADS, Breast Imaging Reporting and Data System; DM, diabetes mellitus; DMP, diabetic mastopathy; US-CNB, ultrasound-guided core needle biopsy

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<https://doi.org/10.1016/j.clinimag.2018.11.002>

Received 3 April 2018; Received in revised form 25 October 2018; Accepted 2 November 2018

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using the keywords ‘diabetic mastopathy’. A total of 12 women with 16 DMP lesions were found, all of which had undergone imaging and had the diagnosis pathologically confirmed.

### 2.1. Mammography and ultrasound

All patients had undergone digital mammograms (LORAD Selenia or Selenia Dimensions, Hologic, Marlborough, MA, USA), using standard mediolateral and craniocaudal views. Additional mammographic views were performed as required. Breast ultrasound was performed on all patients using high frequency linear-array 10–14 MHz transducers (LOGIQ 7 or LOGIQ E9, GE Healthcare, Milwaukee, WI, USA).

### 2.2. Ultrasound-guided core needle biopsy (US-CNB)

US-CNBs were obtained using a 14-gauge automated core needle with a 22-mm throw (Bard®Magnum® Reusable Core Biopsy System, Bard Medical, Tempe, AZ, USA). At least three cores (range, 3–6) were obtained for each lesion. The retrospective pathological reports were reviewed by a pathologist with 10 years of breast pathology experience.

### 2.3. Analysis of imaging features and medical records

All mammography and ultrasound images were displayed on a picture archiving and communications system (PACS) workstation and reviewed by two radiologists who had 5 and 15 years' experience in breast imaging, using the descriptors from the fifth edition of BI-RADS to arrive at a consensus [19]. We subdivided the BI-RADS hypoechoogenicity term into marked hypoechoogenicity and hypoechoogenicity to allow for comparison with previous studies using the same terminology [20–23]. Patients' clinical information was obtained from their medical record, including the age at onset of DM, sex, clinical presentation, menstruation status, type of diabetes, medical treatment, duration between the diagnosis of DM and the diagnosis of DMP, and diabetic complications. In addition, we reviewed follow up imaging and medical records to evaluate any alteration in lesion size or recurrent disease.

## 3. Results

### 3.1. Clinical information

A total of 12 patients with 16 DMP lesions were identified. Three patients had bilateral lesions. One patient had a recurrent lesion that was pathologically confirmed and was included in our analysis. All of the patients were women. The clinical information obtained from the 12 patients at the first presentation of the disease is summarized in Table 1. The majority of lesions (75%) were palpable. The mean age of onset was 52.4 years (range, 39–77 years). Equal numbers of patients were premenopausal and postmenopausal. Most of the patients (10 patients, 83%) had type 2 DM, while two patients (17%) had type 1 DM. Five of the 10 patients with type 2 DM were being treated with oral hypoglycemics. The remaining type 2 DM patients, and the type 1 DM patients were insulin-dependent (58.3%). The mean duration of DM before the diagnosis of DMP was 16.9 years (range, 5–31 years). Eight patients (66.7%) had diabetic complications; namely, retinopathy (2 patients, 16.7%) or both retinopathy and nephropathy (6 patients, 50%).

### 3.2. Mammographic and ultrasound features

Mammography was performed on 15 of the 16 DMP lesions. The mammographic features are summarized in Table 2. Most patients had either extremely dense (36.4%) or heterogeneously dense (45.5%) breasts, and a few patients had scattered areas of fibroglandular density (18.2%). The seven DMP lesions (46.7%) that were negative on mammography occurred in both extremely dense and heterogeneously dense

**Table 1**

Clinical information of the 12 patients with DMP included in this study.

Feature	Number (%)
Menopausal state	
Premenopausal	6 (50)
Postmenopausal	6 (50)
DM type	
Type 1	2 (17)
Type 2	10 (83)
DM medications	
Insulin	7 (58.3)
Oral drug therapy	5 (41.7)
DM complications	
None	4 (33.3)
Retinopathy	2 (16.7)
Retinopathy and nephropathy	6 (50)
Palpability (16 lesions)	
No	4 (25)
Yes	12 (75)

DM, diabetes mellitus; DMP, diabetic mastopathy.

**Table 2**

Mammographic and ultrasound features of the 16 DMP lesions detected in the 12 patients included in this study.

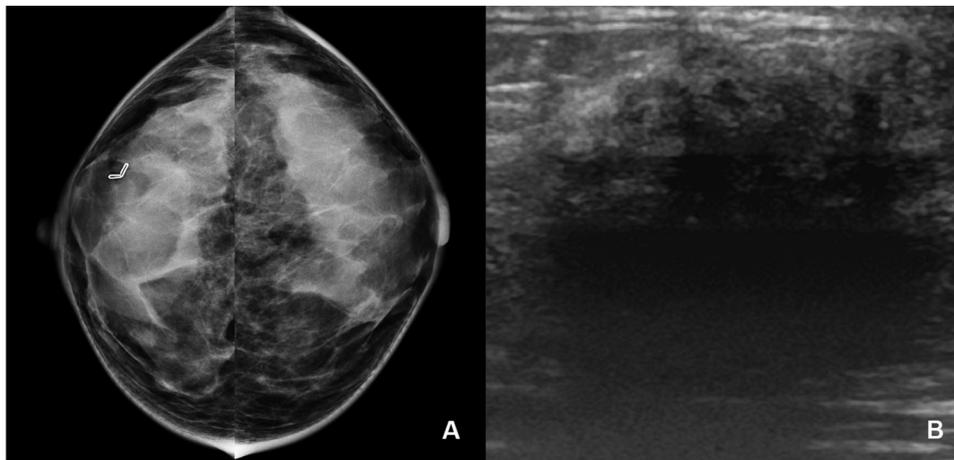
Feature	Number (%)
<i>Mammography</i>	
Breast composition (n = 11)	
Extremely dense	4 (36.4)
Heterogeneously dense	5 (45.5)
Scattered areas of fibroglandular density	2 (18.2)
Mammographic features (n = 15)	
None	7 (46.7)
Focal asymmetry	6 (40)
Asymmetry	2 (13.3)
<i>Ultrasound</i>	
Ultrasound mass features (n = 16)	
Shape	
Irregular	13 (81.3)
Oval	3 (18.8)
Margin	
Indistinct	16 (100)
Orientation in relation to the chest wall	
Parallel	15 (93.8)
Antiparallel	1 (6.3)
Echogenicity	
Markedly hypoechoic	14 (87.5)
Hypoechoic	2 (12.5)
Posterior features	
Shadowing	10 (62.5)
Combined pattern	6 (37.5)
Vascularity <sup>a</sup> (n = 10)	
No	10 (100)
Yes	0
<i>BI-RADS</i> (n = 16)	
4B	5 (31.3)
4C	11 (68.8)

BI-RADS, Breast Imaging Reporting and Data System; DMP, diabetic mastopathy.

<sup>a</sup> The only 10 of the 16 lesions were examined using color Doppler ultrasound.

breasts (Fig. 1). Eight lesions (53.3%) were identified that had abnormal mammographic features, including focal asymmetry and asymmetry (Fig. 2), as defined according to the fifth edition of BI-RADS. None of the lesions had suspicious calcifications or architectural distortion.

Ultrasound was performed on all 16 DMP lesions. The ultrasound features are summarized in Table 2. The mean size of the DMP lesions was 3.0 cm (range, 1.1–6.0 cm). All of the 16 lesions were identified as

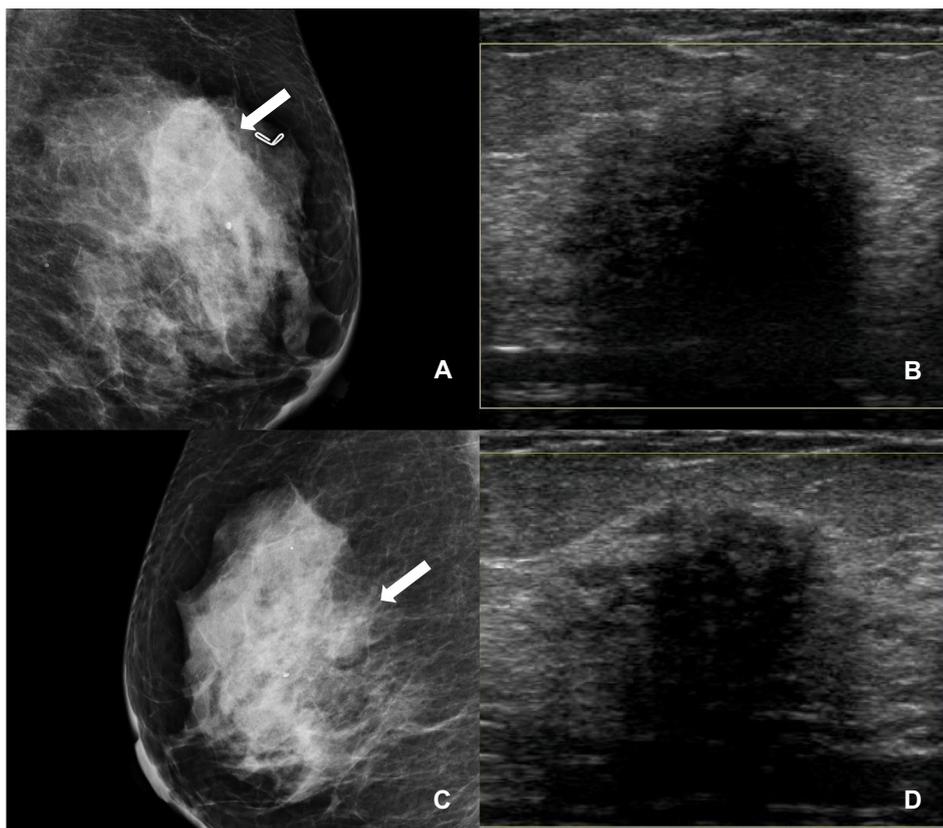


**Fig. 1.** Mammography and ultrasound images from a 44-year-old woman with type 1 DM, presenting with a palpable lump in her right breast.

A. Craniocaudal views on mammography showing extremely dense breasts without focal findings. A metallic staple has been placed in the palpable area of the right breast.

B. Transverse ultrasound showing a 3.7-cm markedly hypoechoic mass with indistinct margins and posterior shadowing corresponding to the palpable area in the right breast.

US-CNB and excision were performed, and the pathological specimen was diagnosed as DMP. DMP, diabetic mastopathy; US-CNB, ultrasound-guided core needle biopsy.



**Fig. 2.** Mammography and ultrasound images from a 57-year-old woman with type 2 DM, who presented with a palpable lump in her left breast.

A. Left mediolateral (MLO) view on mammography showing asymmetry of the superior left breast (arrow).

B. Transverse color Doppler ultrasound shows a 2.6-cm markedly hypoechoic mass, with indistinct margins and posterior shadowing corresponding to the area of asymmetry on mammography and a palpable lump. This mass had no internal vascularity. US-CNB was performed and the pathological report showed benign breast tissue with focal lymphocytic infiltration. Excision was performed, and the pathological specimen was diagnosed as DMP. Over the next 24 months, the patient developed a new palpable lump at her contralateral breast (images presented in C and D).

C. Right MLO view on mammography showing asymmetry of the central right breast (arrow).

D. Transverse color Doppler ultrasound showing a 1.6-cm markedly hypoechoic mass that is similar to the initial lesion in the left breast (B). US-CNB was performed and the pathological report showed benign breast tissue with dense stroma. Due to this non-specific pathology, excision was performed and the pathological specimen was diagnosed as DMP.

DMP, diabetic mastopathy; US-CNB, ultrasound-guided core needle biopsy.

masses on ultrasound. The key ultrasound features were an irregular shape (81.3%), indistinct margins (100%), parallel orientation to the chest wall (93.8%), marked hypoechoogenicity (87.5%), and posterior shadowing (62.5%) as shown in [Figs. 1 and 2](#). The 10 lesions that were examined by color Doppler ultrasound showed no signs of vascularity. None of the patients had enlarged axillary lymph nodes. The ultrasound features of the lesions were classified as BI-RADS 4: either 4B (31.3%) or 4C (68.8%).

### 3.3. Pathologic assessment, follow-up, and recurrence

The pathology results, follow-up information, and recurrences in 16 DMP lesions are summarized in [Table 3](#). US-CNB was used for pathological diagnosis of 14 of the lesions, and the mean number of cores taken was 4.9 (range, 3–6). Most of the lesions (10 lesions, 71.4%) were definitively diagnosed as DMP based on the pathology results from the

initial US-CNB. In contrast, four lesions that were sampled using US-CNB had a discordant imaging-pathological correlation and the lesions were surgically excised for further examination. The other two breast lesions were diagnosed after excision. Photographs taken from a representative pathology specimen are shown in [Fig. 3](#).

Ten of the 16 DMP lesions were followed-up using ultrasound for a mean period of 40.4 months (range, 21–64 months) after they were pathologically diagnosed as DMP. Three of the lesions increased in size, three disappeared, and four remained the same size. The three DMP lesions that increased in size did not have repeat biopsies. After an initial increase in size, these lesions remained stable over a mean follow-up time of 26.3 months (range, 12–43 months). Three patients (30%) developed five new lesions between them: four of these were in the contralateral breast to the original lesion and one lesion was in the ipsilateral breast. The mean time period for these new lesions to be detected after the initial diagnosis was 34.4 months (range,

**Table 3**  
Pathological diagnosis, follow-up, and recurrences in the 12 patients with 16 DMP lesions included in this study.

Lesion number	Number of CNB cores taken	CNB results	Correlation of CNB results with imaging results	Excision results	Follow-up interval (months)	Follow-up results	New lesions detected on follow-up
1	5	Benign breast tissue	Discordant	DMP	30.5	Increased	No
2	–	–	–	DMP	28.5	Disappeared	No
3	6	DMP	Concordant	–	21	Same size	No
4	5	DMP	Concordant	–	21	Same size	No
5	4	DMP	Concordant	–	–	–	–
6	5	DMP	Concordant	–	–	–	–
7	3	DMP	Concordant	–	–	–	–
8	5	DMP	Concordant	DMP	–	–	–
9	6	DMP	Concordant	–	–	–	–
10	5	DMP	Concordant	–	–	–	–
11	5	Benign breast tissue with relatively dense stroma, non-specific	Discordant	DMP	44	Increased	3 new lesions; 1 lesion in ipsilateral breast (after 38 months) and 2 lesions in contralateral breast (after 44 months)
12	4	Benign breast tissue with focal lymphocytic infiltration	Discordant	DMP	64	Disappeared	1 lesion in contralateral breast (after 24 months)
13	4	Benign breast tissue with dense stroma	Discordant	DMP	40	Disappeared	No
14	–	–	–	DMP	62	Same size	1 lesion in contralateral breast (after 22 months)
15	6	DMP	Concordant	DMP	46.5	Increased	No
16	6	DMP	Concordant	DMP	46.5	Same size	No

DMP, diabetic mastopathy; CNB, core needle biopsy.

22–44 months). Only one of the new lesions was biopsied. The remaining new lesions had imaging features similar to those of the initial DMP lesions and remained stable in size after their initial detection over a mean follow-up time of 22.5 months (range, 18–30 months). During the follow-up period, none of the patients developed breast cancer.

**4. Discussion**

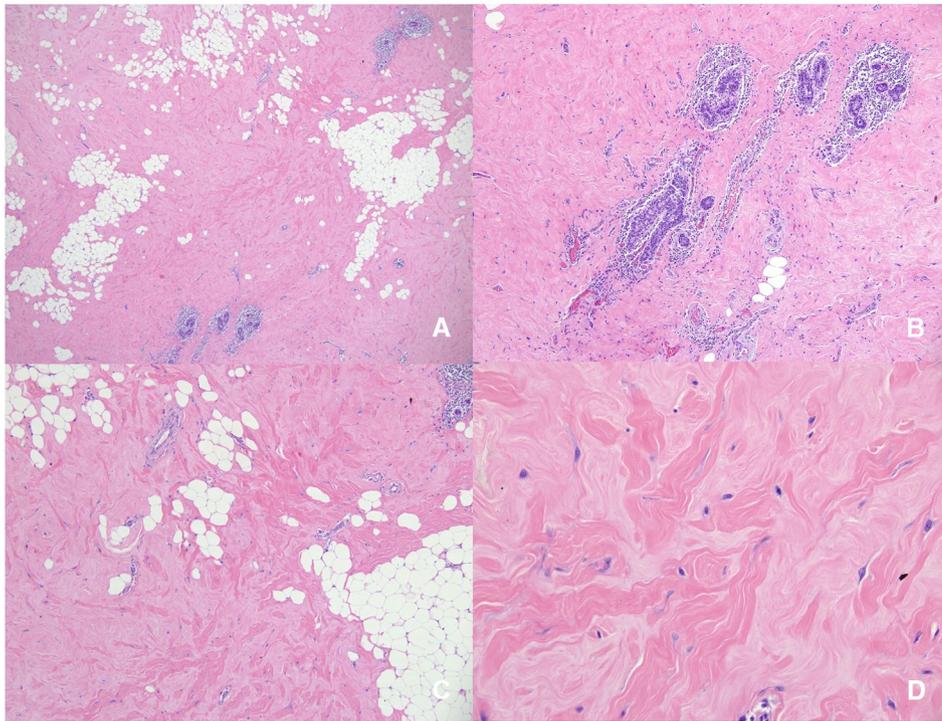
DMP is a rare benign fibrotic disease of unknown etiology and pathophysiology. It has been hypothesized that prolonged hyperglycemia is an influential factor that induces glycosylation and results in excessive levels of glycosylated end products. This promotes an immune reaction that causes extracellular matrix expansion due to elevated collagen production and decreased protein degradation [1,2,15]. In our study, the mean duration of DM before initial diagnosis of DMP was 16.9 years, which supports this hypothesis. The long duration of disease may be the reason that the majority of the patients (66.7%) had diabetic complications, including retinopathy and nephropathy. This finding is similar to those of previous studies [7,12,24,25].

Most studies from Western countries have found that DMP is associated with long-standing type 1 DM, while it rarely occurs in patients with type 2 DM [1,2,7]. In contrast, we found that the majority of the patients in our study had type 2 DM (83%), while a smaller number had type 1 DM (17%). The mean age of onset among our patients was 52.4 years and half of the patients were postmenopausal. This finding is also not consistent with previous studies from Western countries, which have reported that DMP usually occurs in younger premenopausal women [1,2,7]. However, our results which were studied in Thailand are similar to the results obtained from research in Asian populations [24–26]. These studies also found that DMP is more prevalent in older patients, and more so in those with type 2 DM rather than type 1 DM. This discrepancy could be explained by a low prevalence of type 1 DM in Asia in comparison with the West, as well as a trend towards an increased prevalence of type 2 DM in Asia [27,28].

Interestingly, we found that the proportion of DMP patients who were insulin-dependent (58.3%) was slightly higher than the proportion that used oral hypoglycemics (41.7%). Previous studies have also found an increased prevalence of DMP among patients with type 2 DM who were insulin-dependent than in those that used oral hypoglycemics [4,24,25]. It appears that type 2 DM patients often become insulin-dependent as their disease progress. Therefore, insulin-dependent is probably to be associated with long-standing diabetes that was found as the typical characteristic of our DMP patients. In addition, there is a possibility that the insulin treatment itself is a predisposing factor of DMP. However, this later hypothesis should be further investigated in larger populations.

Most of the patients in our study had dense breasts (81.9%), which were classified as extremely dense or heterogeneously dense. On mammography, nearly half of the lesions (46.7%) had negative findings and the remaining positive features were classified as focal asymmetry and asymmetry, as defined by BI-RADS. Our results are the same as in other studies [2,14,29], which found that common mammographic features of DMP are dense breast tissue parenchyma or asymmetry. Mammographically dense breast tissue may obscure DMP and reduce the sensitivity of its detection [30,31]. In our study, the mean size of DMP lesions with negative findings on mammography was 3.9 cm (range, 2.2–6.0 cm). In contrast, the size of occult breast cancer lesions in mammographically dense breasts is usually < 1.2 cm [32–34]. Therefore, the fact that large-sized DMP lesions can be occult on mammography may help to differentiate DMP from invasive cancer, especially in there is a history suggestive of DMP.

The common ultrasound features in our studies were irregular shape, indistinct margins, marked hypoechoogenicity, parallel orientation to the chest wall, posterior shadowing, and absent vascularity. These features are consistent with those identified by several previous studies [2,7,25,29,35]. Marked hypoechoogenicity and posterior



**Fig. 3.** Histopathological findings of diabetic mastopathy. A. Perilobular and periductal infiltration by lymphocytes with dense hyalinized stroma (H&E  $\times$  40). B. Dense perilobular and periductal infiltration by small lymphocytes without ductal proliferation (H&E  $\times$  100). C. Thick hyalinized collagen bundles noted in the stroma (H&E  $\times$  100). D. Epithelioid spindle cells noted among the collagen bundles (H&E  $\times$  200). DMP, diabetic mastopathy.

shadowing in DMP are most likely explained by the extensive fibrotic component of the disease. Moreover, parallel orientation and absent vascularity of the masses are signs of benign lesions which might be positive predictors of DMP out of malignancy. However, the other ultrasound features of DMP resemble those of invasive cancers, particularly low-grade or Luminal-A subtypes of invasive ductal carcinoma and invasive lobular carcinoma [36–39]. As a result, the ultrasound features of DMP are often classified as BI-RADS category 4, in agreement with the results in our study. Therefore, tissue sampling is required to exclude malignancy.

As described above, tissue sampling is currently required for the pathological diagnosis of DMP because imaging features alone cannot accurately exclude malignancy. However, previous studies have shown that excision of DMP should be avoided because surgery can stimulate progression and there is a high rate of recurrence after resection [1,25]. Our study revealed that US-CNB successfully diagnosed DMP in 10/14 lesions (71.4%). A few previous studies [7,13,25] have also found that US-CNB is a useful tool for the diagnosis of DMP when correlated with the clinical history. If necessary, further tissue sampling could be carried out for discordant imaging-pathology lesions after discussion in multidisciplinary team that includes the referring physician, radiologist, pathologist, and breast surgeon. Further sampling could include repeat US-CNB, vacuum-assisted biopsy, or surgical excision [25]. After diagnosis as benign disease, the patient should be advised about the natural history of DMP and be followed-up with routine imaging [40]. Repeat US-CNB should be considered if new suspicious lesions are detected or if there is clinical concern [13].

In our study, 10 DMP lesions were followed-up with imaging and eight DMP lesions were surgically excised. Three of the eight lesions (37.8%) increased in size after excision, and one patient developed new disease adjacent to the resected site, suggesting that surgical resection may have exacerbated the disease, as reported previously [1,2,16]. Five new lesions were detected in three of our patients on follow-up. These occurred in the ipsilateral or contralateral breast to the initial lesion within 4 years of the original diagnosis.

DMP is a rare disease; therefore, our study was retrospective and included only a small number of patients. Moreover, the patient population used in this study was from a single tertiary hospital in

Thailand and may not be representative of populations elsewhere. The DMP patients were selected from a database of pathology reports; therefore, any patients that did not have tissue biopsies because they had DMP lesions with benign imaging features were not included in this study. The follow-up period of our study was also relatively short, and the follow-up data were incomplete because our tertiary hospital usually sent patients for follow-up at their nearest hospitals and the data from these patients could not be obtained. Also, seven of the eight DMP lesions that increased in size or appeared *de novo* at follow-up were not biopsied to confirm the diagnosis of DMP, although they were stable in size at follow-up  $\geq$  12 months. Together, these limitations may have biased our interpretations of the disease outcomes in this study.

## 5. Conclusions

DMP is a rare benign fibrotic disease that occurs in patients with a prolonged duration of DM that often have complications of long-standing DM. In our study, DMP was much more common in patients with type 2 DM and those that were insulin-dependent. The ultrasound features of DMP mimicked those of malignancy and were classified as BI-RADS category 4, deeming it necessary to perform tissue biopsy for diagnosis. In contrast, the mammographic features were usually occult, despite the often large sizes of DMP lesions. When correlated with the clinical context and managed using a multidisciplinary approach, use of US-CNB allows avoidance of surgical excision that can exacerbate the disease.

## Conflicts of interest

The authors hereby declare no personal or professional conflicts of interest regarding any aspects of this study.

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