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ORIGINAL ARTICLE

Breast Manifestations in Patients with Systemic Lupus Erythematosus

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ABSTRACT

Objectives: *Breast manifestations in patients with systemic lupus erythematosus (SLE) include primary lupus of the breast (i.e., lupus mastitis) and secondary manifestations of lupus such as lymphadenopathy or vascular calcifications. To clarify the spectrum of breast manifestations in patients with SLE, we reviewed the clinical, imaging, and pathological manifestations of breast diseases in SLE patients.*

Methods: *We retrospectively reviewed cases of SLE patients with breast imaging performed in five centres from January 2010 to April 2020. Patient demographics, breast symptoms, imaging, and pathological findings, and their subsequent management, were reviewed.*

Results: *A total of 16 cases were included. The mean follow-up period was 61 months. A palpable breast mass was the most frequent clinical presentation, followed by mastalgia and axillary swelling. A wide range of imaging findings was encountered on ultrasonography and/or mammography, including extensive calcifications in both breasts, breast masses with features suspicious for malignancy, fat necrosis, oedema, arterial calcifications, architectural distortion, and axillary lymphadenopathy. Two cases of lupus mastitis and a case of invasive ductal carcinoma were identified.*

Conclusion: *No definite distinguishing features between lupus mastitis and breast malignancy were observed on imaging. Pathological correlation is recommended when imaging features suspicious for malignancy are demonstrated.*

Key Words: *Lupus erythematosus, systemic; Magnetic resonance imaging; Mammography; Mastitis; Ultrasonography*

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中文摘要

系統性紅斑狼瘡患者的乳腺表現

周朗妍、黃婷、周智敏、陳樂詩、陳庭笙、雷彩如、翁維德、馮小玲、馬嘉輝

目的：系統性紅斑狼瘡（SLE）患者的乳腺表現包括乳腺原發性狼瘡（即狼瘡性乳腺炎）和狼瘡的繼發性表現，例如淋巴結腫大或血管鈣化。為了闡明SLE患者的各種乳腺表現，本研究回顧SLE患者乳腺疾病的臨床、影像學和病理學表現。

方法：回顧性分析2010年1月至2020年4月期間在五間醫療中心進行乳腺成像的SLE患者病例。回顧患者的人口統計學、乳腺症狀、影像學和病理學及其後續處理。

結果：共納入16例。平均隨訪期為61個月。最常見的臨床表現是可觸及的乳腺腫塊，其次是乳腺痛和腋窩腫脹。在超聲檢查和／或乳腺X光檢查中發現各種影像學表現，包括雙側乳腺廣泛鈣化、乳腺腫塊具可疑惡性腫瘤特徵、脂肪壞死、水腫、動脈鈣化、結構變形和腋窩淋巴結腫大。病例中有2例狼瘡性乳腺炎和1例浸潤性導管癌。

結論：影像學上未觀察到狼瘡性乳腺炎與乳腺惡性腫瘤之間的明確區分特徵。 當發現可疑惡性腫瘤的影像特徵時，建議進行病理學相關檢查。

INTRODUCTION

Systemic lupus erythematosus (SLE) is a complex autoimmune disease with multisystem involvement characterised by inflammation, vasculitis, immune complex deposition, and vasculopathy.[1] It is substantially more common in women of childbearing age.[2] Breast diseases in patients with lupus may be primary lupus of the breast (i.e., lupus mastitis) or secondary manifestations of lupus such as lymphadenopathy or vascular calcifications. These patients are also subject to breast diseases unrelated to SLE. To our knowledge, the spectrum of breast manifestations in patients with SLE has not been described in the literature, with case reports mainly focusing on lupus mastitis. To clarify the spectrum of breast manifestations in patients with SLE, we retrospectively reviewed the clinical, imaging, and pathological findings in patients with SLE.

METHODS

Cases of SLE with breast imaging (mammography, ultrasound, or magnetic resonance imaging [MRI]) in five centres from January 2010 to April 2020 were identified through a search of the Radiology Information System using the keywords 'lupus', 'SLE', and 'systemic lupus erythematosus'. Cases without breast imaging or with unavailable imaging were excluded.

Sixteen cases were found; all had available breast imaging studies. Case demographics, breast symptoms, breast imaging findings, pathological findings (if any) and subsequent management were reviewed.

RESULTS

Patient Demographics

In total, 16 cases of SLE were identified and included for analysis. No cases were excluded. The mean age of presentation of breast symptoms was 44 years (range, 23-71). The mean duration of SLE at time of breast disease presentation was 11.2 years. Breast symptoms occurred after diagnosis of SLE in 14 of the 16 cases. Breast symptoms occurred before diagnosis of SLE in the remaining two cases, and among them one presented with a breast mass 2 years before the diagnosis of SLE. One patient presented with bone pain and weight loss, and breast imaging was performed at the same time as part of the systemic investigation for SLE (Figure 1). The mean follow-up period was 61 months.

Clinical Presentation

Among the 16 patients, palpable breast mass was the most common clinical presentation in nine (56%) patients, followed by mastalgia in three (19%) patients and axillary swelling in two (13%) patients. One (6%) patient presented with a palpable breast mass and axillary swelling, and one (6%) patient presented with bone pain and weight loss.

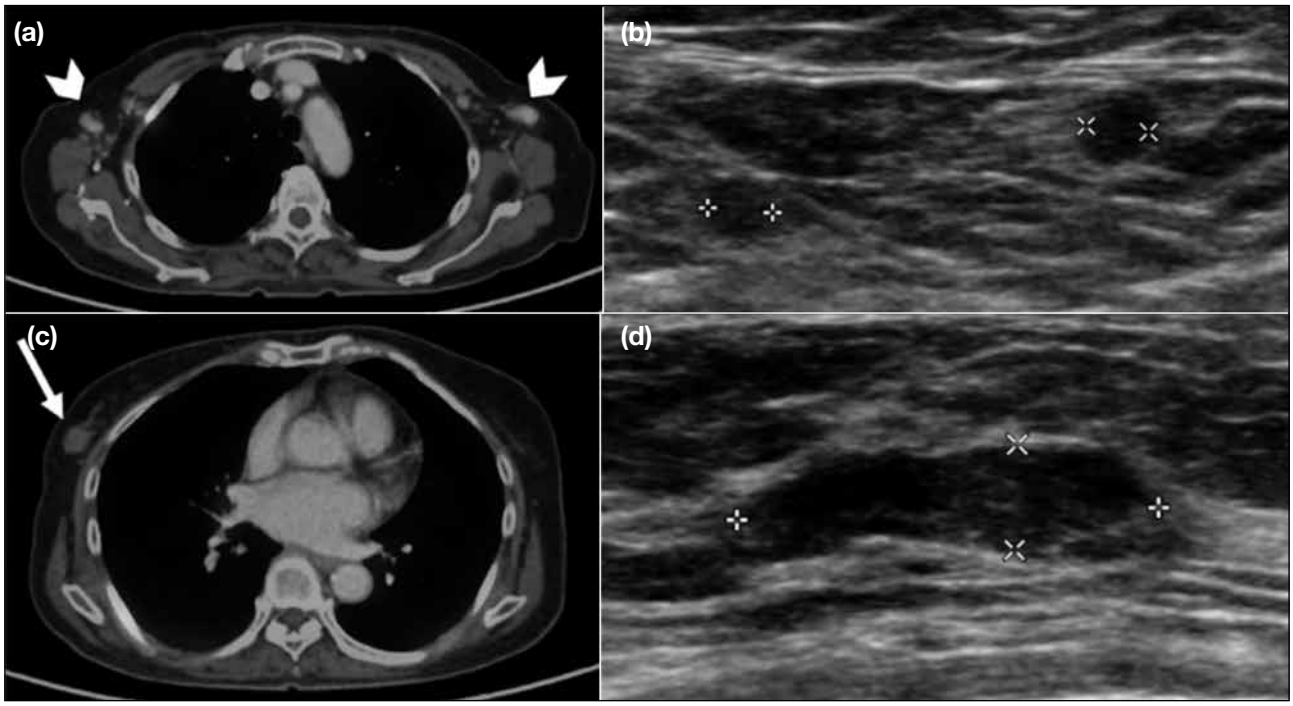

Figure 1. ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) images and corresponding ultrasonograms from a patient presenting with bone pain and weight loss. (a) PET/CT scans through the axillae reveal multiple prominent bilateral axillary lymph nodes with hypermetabolism (SUVmax 3.6) (arrowheads). (b) Ultrasonogram showing suspicious lymph nodes with loss of fatty hila, which were targeted for fine needle aspiration. Cytology confirmed reactive lymph nodes. (c) PET/CT images show a non-hypermetabolic (SUVmax 1.0) breast mass in the upper outer quadrant of the right breast on (arrow). (d) Ultrasonogram showing a mildly irregular hypoechoic mass corresponding to the lesion on PET/CT. Biopsy revealed a fibroadenoma.

Investigations

One (6%) patient underwent mammography, ultrasonography, and MRI scans, eight (50%) patients underwent mammography and ultrasonography, six (38%) patients underwent ultrasonography only, and the remaining one (6%) patient underwent mammography only. In total, ultrasonography of the breasts was performed in 15 (94%) of the 16 cases.

Imaging Findings

Imaging findings included breast mass, calcifications, fat necrosis, architectural distortion, breast oedema, and axillary lymphadenopathy (Table).

Lupus Mastitis

There were two cases of lupus mastitis with pathological confirmation. Both patients presented with a palpable breast mass. In the first case, extensive calcifications were seen both on mammography and ultrasound and the patient subsequently underwent core biopsy (Figure 2). Pathology showed hyaline fat necrosis, nodular perilobular and perivascular inflammatory infiltrate comprising lymphocytes and plasma cells, and stromal fibrosis with microcalcifications, compatible with lupus mastitis. The patient was treated with systemic steroids and immunosuppressants as part of her therapy for SLE. During >6 years of clinical and imaging follow-up examinations, the calcifications remained stable and the patient did not have recurrence of lupus mastitis symptoms. No further biopsy was performed.

In the second case (Figure 3), an irregular high-density retroareolar mass with indistinct margins was present in the right breast on mammography, with ultrasound showing a corresponding irregular infiltrative hypoechoic mass with associated parenchymal oedema. It was classified as highly suspicious for malignancy. Vacuum-assisted biopsy was performed in this case with pathology confirming lupus mastitis.

Ultrasound and MRI scans were performed 5.5 years later in view of persistent breast symptoms. MRI scans showed a heterogeneous retroareolar mass on T2-weighted images with associated skin thickening and mild breast oedema, which was proven to be lupus mastitis on previous biopsy. Areas of signal suppression

Table. Imaging findings.

Imaging findings			No. of patients (No. of masses)	Pathology (if available)
Breast mass	Suspicious for malignancy (BI-RADS 4)	Irregular hypoechoic mass with spiculated margins and associated pleomorphic microcalcifications	1 (1)	Invasive ductal carcinoma
		Irregular infiltrative hypoechoic mass	1 (1)	Lupus mastitis
		Mildly irregular hypoechoic mass	1 (1)	Fibroadenoma
		Mildly irregular hypoechoic mass with coarse calcifications	1 (1)	Fibroadenoma
	Probably benign (BI-RADS 3)	Oval hypoechoic mass with circumscribed margin	6 (13)	FNA performed for 6 of the 13 masses: 5 showed fibroadenoma, 1 was insufficient for diagnosis
	Benign (BI-RADS 2)	Breast cyst	2	
Calcifications	Extensive coarse calcifications in both breasts (BI-RADS 2)		2	Biopsy of 1 case: lupus mastitis. FNA for the other case: no malignancy
	Arterial calcifications (BI-RADS 2)		3	
	Group of pleomorphic microcalcifications associated with a spiculated breast mass (BI-RADS 4)		1	Invasive ductal carcinoma
	Group of punctate microcalcifications (BI-RADS 3)		1	
	Benign scattered microcalcifications (BI-RADS 2)		1	
Fat necrosis	Fat-containing lesion with peripheral enhancement on MRI scan (BI-RADS 2)		1	Lupus mastitis
Architectural distortion	Architectural distortion likely surgical scar (BI-RADS 2)		2	Biopsy performed for 1 case: no malignancy
Breast oedema	Unilateral breast oedema associated with infiltrative breast mass (BI-RADS 4)		1	Lupus mastitis
Axillary lymphadenopathy	Axillary lymph nodes with thickened cortex		2	
	Axillary lymph nodes with loss of fatty hilum		1	Reactive lymphadenopathy
	Multiple prominent axillary lymph nodes without suspicious features		4	FNA for 3 of the 4 lymph nodes: 1 showed no malignancy; the other 2 were insufficient for diagnosis

Abbreviations: BI-RADS = Breast Imaging Reporting and Data System; FNA = fine needle aspiration; MRI = magnetic resonance imaging.

with peripheral enhancement within the mass on the T1-weighted fat-saturated sequence were suggestive of fat necrosis, compatible with the pathological process of lupus panniculitis. The peripheral enhancement showed a progressive enhancement pattern suggestive of a type 1 kinetic curve.[3] Ultrasound findings were static, and the patient remained stable with medical therapy of SLE.

Breast Mass with Suspicious Imaging Features for Malignancy

Apart from the previously mentioned cases of pathologically confirmed lupus mastitis, there were three other breast masses with suspicious imaging features for malignancy in our patient cohort. One of them was proven to be invasive ductal carcinoma, while the other two were fibroadenomas.

The invasive ductal carcinoma (Figure 4) was highly suspicious for malignancy (Breast Imaging Reporting and Data System [BI-RADS] 4C) on imaging. On mammography, there was a spiculated mass with associated fine pleomorphic microcalcifications. On ultrasonography, a corresponding irregular hypoechoic mass with spiculated margin and posterior acoustic shadowing was detected. Core biopsy was performed and yielded invasive ductal carcinoma. The patient subsequently underwent mastectomy and axillary dissection with adjuvant chemotherapy.

The fibroadenomas were slightly irregular masses with and without internal coarse calcifications.

Probably Benign Oval Circumscribed Hypoechoic Breast Masses

Oval circumscribed hypoechoic masses on ultrasonography, which were classified as probably

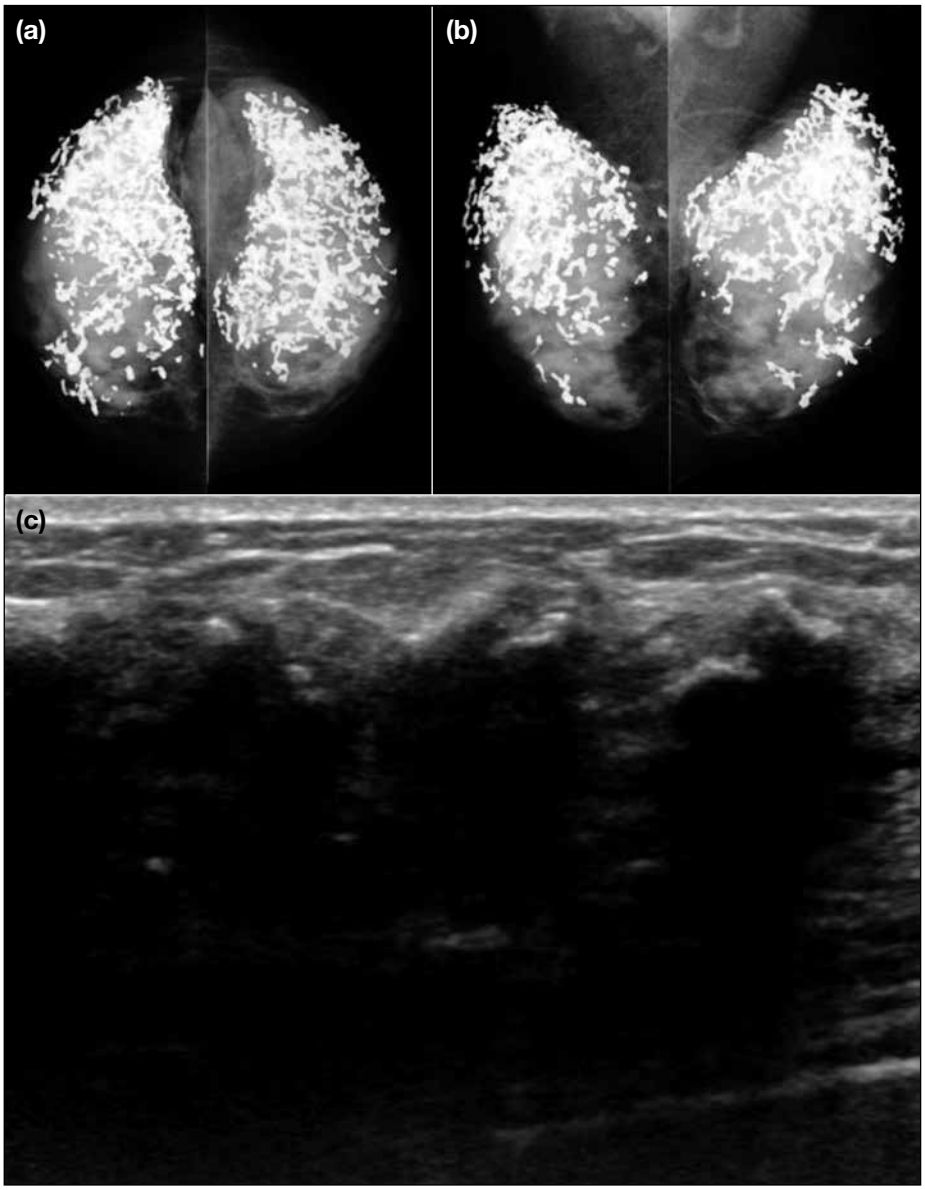

Figure 2. Imaging findings of a patient with lupus mastitis. (a, b) Craniocaudal (a) and mediolateral oblique (b) mammograms showing extensive coarse calcifications of both breasts. (c) Ultrasonogram showing diffuse coarse calcifications of both breasts.

benign (BI-RADS 3), were the most commonly encountered breast manifestation in our cases, with 13 masses observed in six of the patients (Figure 5). Fine needle aspiration (FNA) was performed for six of these 13 masses, yielding fibroadenoma for five of the cases. One of these masses showed mild interval enlargement on new ultrasonography at 6 months; results of a new core biopsy showed no malignancy. The remaining one case with FNA performed showed inconclusive results as the FNA sample was insufficient for diagnosis; this patient was followed up clinically and with breast ultrasound for >3 years, showing stability of the oval hypoechoic masses. All of the 13 oval circumscribed hypoechoic masses were followed up with breast imaging, with the exception of the aforementioned mass that showed mild interval enlargement, the other 12 masses all showed stability with range of follow-up period from 3.5 years to 7 years, thus classified as benign.

Calcifications

We encountered two cases of extensive calcifications in both breasts; one was the case of lupus mastitis (Figure 2) described above, while the other case showed no malignancy by FNA.

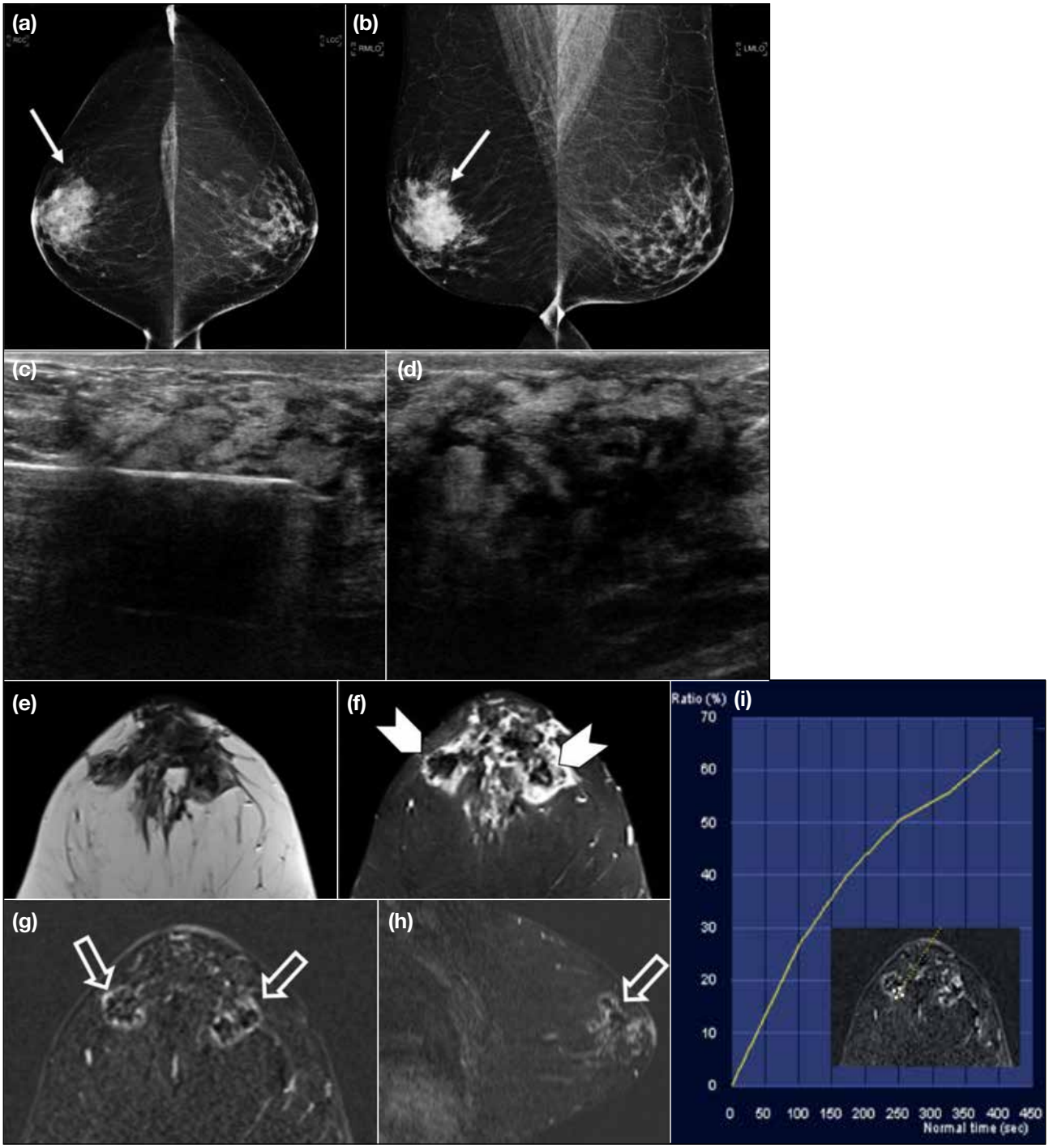

Figure 3. Imaging findings of another patient with lupus mastitis. (a, b) Craniocaudal (a) and mediolateral oblique (b) mammograms showing an irregular high-density retroareolar mass with indistinct margins in the right breast (arrows). (c, d) Images from vacuum-assisted biopsy under ultrasound guidance showing an irregular infiltrative hypoechoic mass with indistinct margins and associated parenchymal oedema. Biopsy result confirmed lupus mastitis. (e-h) Magnetic resonance imaging performed 5.5 years after the initial investigations, with sequences including (e) axial T2-weighted; (f) axial T1-weighted with fat saturation; (g) axial subtracted contrast-enhanced T1-weighted; and (h) sagittal reconstruction contrast-enhanced T1-weighted sequences showing areas of hypointense signals on T1-weighted sequence with fat saturation (f: arrowheads) in the retroareolar mass with peripheral enhancement (g, h: open arrows), compatible with areas of fat necrosis. (i) Analysis of the area of enhancement showing a type 1 progressive enhancement pattern, usually indicating benignity.

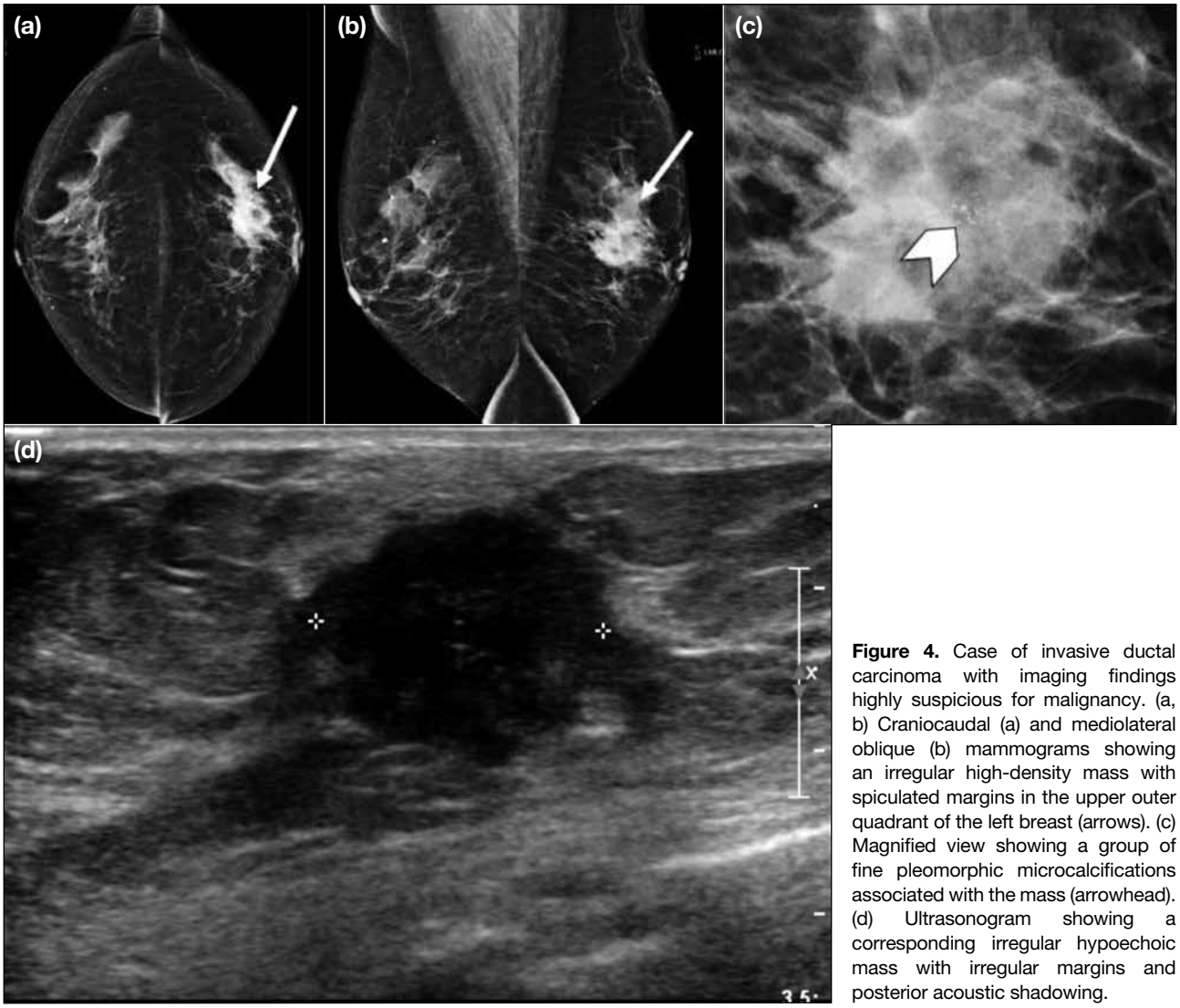

Figure 4. Case of invasive ductal carcinoma with imaging findings highly suspicious for malignancy. (a, b) Craniocaudal (a) and mediolateral oblique (b) mammograms showing an irregular high-density mass with spiculated margins in the upper outer quadrant of the left breast (arrows). (c) Magnified view showing a group of fine pleomorphic microcalcifications associated with the mass (arrowhead). (d) Ultrasonogram showing a corresponding irregular hypoechoic mass with irregular margins and posterior acoustic shadowing.

Arterial calcifications were observed in three patients. All three patients had a history of lupus nephritis. Two of them did not have traditional risk factors for atherosclerosis, namely hypertension, diabetes mellitus, hyperlipidaemia and obesity, while the other patient had hyperlipidaemia but not known of diabetes mellitus or hypertension.

Other calcifications observed in our patients included groups of fine pleomorphic microcalcifications in association with a spiculated breast mass in the case of invasive ductal carcinoma (Figure 4), a group of punctate microcalcifications that was stable on follow-up, and benign scattered microcalcifications.

Architectural Distortion

Architectural distortion was observed in two of the cases and was likely due to scar related to previous breast surgery. One of the patients had a history of excision of phyllodes tumour and fibroadenoma. The other patient (Figure 6) had undergone previous breast mass excision with pathology showing lupus mastitis. This patient subsequently had core biopsy due to new development of subtle hypoechoic changes on ultrasonography, which corresponded to the site of architectural distortion, with pathology being negative for malignancy. This patient was followed up for 6 years with stable imaging results and without recurrence of breast symptoms suggestive of lupus mastitis.

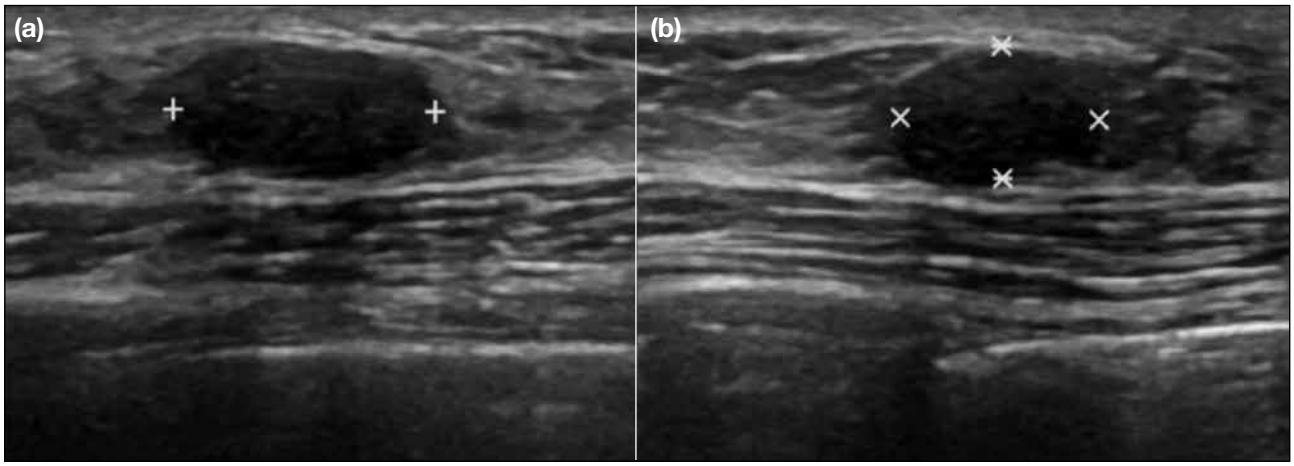

Figure 5. (a, b) Ultrasonogram showing an oval circumscribed parallel hypoechoic mass, which was the most commonly encountered finding in our patient cohort. Fine needle aspiration was performed for this mass with cytology confirming fibroadenoma.

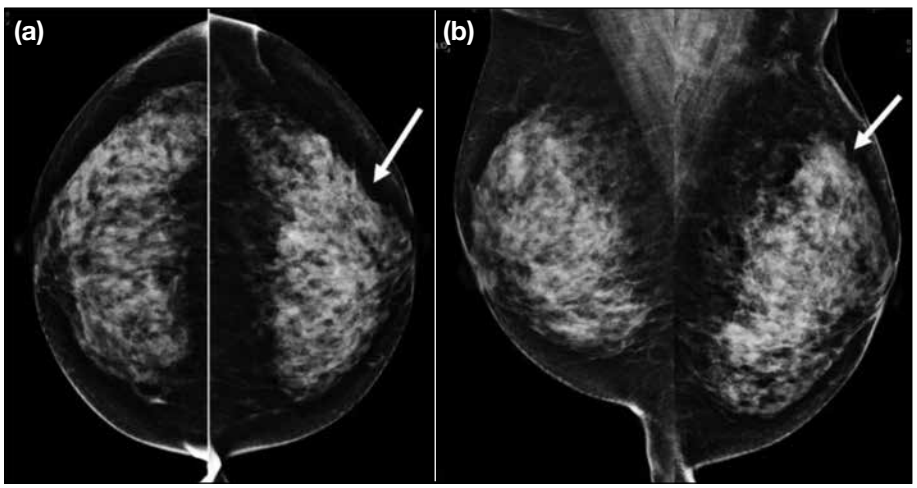

Figure 6. Subtle architectural distortion due to surgical scar on mammography, better seen on (a) craniocaudal view than (b) mediolateral view (arrows). This patient had undergone breast mass excision previously with pathology showing lupus mastitis. She subsequently had core biopsy of the area of architectural distortion due to new development of corresponding hypoechoic changes on ultrasonography, with pathology being negative for malignancy. This patient was followed up for >6 years without recurrence of lupus mastitis.

Axillary Lymphadenopathy

Axillary lymph nodes with suspicious features such as thickened cortex and/or loss of fatty hila were present in three patients (Figure 7). FNA was performed for one patient with cytology being reactive lymphadenopathy. FNA was not performed for the other two cases with suspicious axillary lymph nodes as the patient refused for one case and clinical features were not suspicious for the other case. Multiple axillary lymph nodes without suspicious imaging features were observed in four patients. Three patients underwent FNA of lymph nodes with one of them showing no evidence for malignancy, while the other two samples were insufficient for diagnosis. All of the cases, including those with suspicious features, showed stability on follow-up ultrasound with follow-up period of 15 months to 8 years.

DISCUSSION

Our review showed that a wide spectrum of generally nonspecific sonographic and mammographic findings can be present in patients with SLE. Some are due to SLE, including primary lupus of the breast (i.e., lupus mastitis) and secondary manifestations of SLE such as lymphadenopathy or vascular calcifications. Other findings, such as breast cancer, are not known to be lupus-related and can occur in women unaffected by lupus.

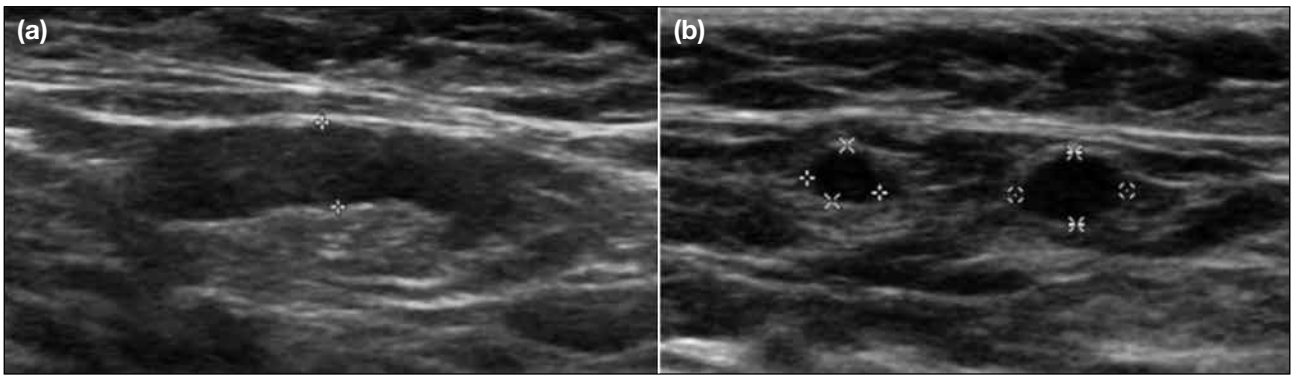

Figure 7. Axillary lymph nodes with (a) thickened cortex (0.55 cm) and (b) loss of fatty hila, which are both suspicious sonographic features of pathological process. Fine needle aspiration of the lymph node shown in (a) was refused by the patient. Fine needle aspiration of the lymph nodes shown in (b) showed reactive lymphadenopathy.

Lupus Mastitis

Lupus mastitis is a subset of lupus panniculitis that is localised to the breast and is a rare manifestation of SLE. Lupus panniculitis is a rare chronic inflammatory reaction of the subcutaneous fat that can occur in 2% to 3% of patients with SLE, usually between age 20 and 50 years, and more common in women than in men.[4-6]

Clinically, lupus mastitis can occur in patients with an established diagnosis of SLE or can rarely be the first manifestation of the disease.[5] In both cases of lupus mastitis in our cohort, SLE was established before the onset of breast symptoms. The most common presentation is a palpable lesion, often associated with pain,[7] as in both of our cases. The overlying skin may be normal but cutaneous changes such as erythema, hyperkeratosis, lipoatrophy or even ulceration can be evident.[5] Diffuse breast enlargement and palpable axillary lymph nodes are less common.[7] The clinical course of lupus mastitis is often chronic with flares and remissions.[6]

For histopathological diagnosis, the major criteria are fat hyaline necrosis, lymphocytic infiltration with lymphoid nodules surrounding the necrosis, periseptal or lobular panniculitis, and microcalcifications. Minor criteria are changes of discoid lupus erythematosus in the overlying skin, lymphocytic vasculitis, mucin deposition, and hyalinisation of subepidermal papillary zones. The combination of four major and four minor criteria is virtually diagnostic and permits differentiation from other forms of panniculitis.[8]

In our two cases of confirmed lupus mastitis, one patient had extensive macrocalcifications in both breasts on imaging, while the other had an infiltrative irregular breast mass. Mammography, ultrasonography, and MRI scans are used as imaging investigations for lupus mastitis, as for other breast diseases. Various imaging findings of lupus mastitis have been described,[4,7,9-14] depending on the stages of fat necrosis.

On mammography, large, dystrophic calcifications are the most commonly encountered findings, as in one of our cases.[7] Early mammographic findings include thin curvilinear calcifications that, on subsequent images, progressively enlarge and coarsen, mirroring the pathologic evolution of focal panniculitis to maturing subcutaneous fat necrosis.[9] Early calcifications frequently simulate malignancy and present in a ductal distribution or appear fine linear-branching in morphology. As fat necrosis progresses, the calcifications increase in size and become coarse and benign in appearance and also can often be seen on ultrasound and MRI scans.[10] Lupus mastitis can also present as a mass (often ill-defined) or asymmetry (focal or global) and may mimic carcinoma.[7] Interval increase in mammographic density and decreasing breast size over time can be present due to underlying fibrosis.[11]

Sonographic findings of lupus mastitis also depend on and reflect stages of fat necrosis. The most commonly seen findings on ultrasonography are a hypoechoic ill-defined mass, areas of architectural distortion, or changes in echotexture of the breast that are more hyperechoic due to infiltration of the subcutaneous fat and/or breast parenchyma.[7] In patients who present with a discrete

mass, non-specific features such as solid, irregular, echogenic lesions with ill-defined margins have been described.[5,6,13] Cutaneous involvement has also been described and it is postulated to result from increased vascularity in the subcutaneous plane, which may also affect deeper planes than in the dermis.[4,7] These findings may mimic those of advanced breast carcinoma with skin involvement. Calcifications with marked posterior acoustic shadowing can be seen on ultrasonography when dystrophic calcifications due to fat necrosis are present.

MRI is infrequently used for the evaluation of lupus mastitis. The MRI features of lupus mastitis are nonspecific and MRI can be helpful for showing the extent of the disease and in demonstrating skin involvement as in our case.[4,7,10] Some of the reported MRI findings of lupus mastitis include skin thickening with marked fat stranding, large coarse calcifications seen as low-signal lesions, irregular masses (which can demonstrate fat content) with rim enhancement and a variable enhancement curve. The morphological and kinetic features can be indistinguishable from malignancy.[12-14] High signal intensity within the lesion on pre-contrast scan with fat suppression may be hints for underlying fat necrosis,[12-14] which was also seen in our case of biopsy-proven lupus mastitis. A type 1 kinetic curve was observed in our case, a finding that is usually associated with benignity. As the enhancement pattern for lupus mastitis can be variable, the morphology of lesions on MRI scans is often more informative than the kinetic curve alone. Overall MRI findings were indistinguishable from malignancy, which emphasises that MRI should not be performed to differentiate between lupus mastitis and malignancy, but rather to delineate the extent of known lupus mastitis.

The second case of lupus mastitis displayed extensive coarse calcifications in both breasts on both ultrasonography and mammography. Freehand FNA of both breasts was performed by surgeons before imaging with results showing no malignancy, thus further biopsy was not performed after imaging after discussion with the patient. Therefore, in cases of suspected lupus mastitis where extensive calcifications are present, we suggest core biopsy to allow histological analysis rather than FNA. In addition, the history of SLE should be clearly stated in the request form as this is important to allow pathologists to accurately identify lupus mastitis.

Breast carcinoma, in particular inflammatory breast carcinoma, can show clinical and radiological features similar to those of lupus mastitis, especially in patients who present with a rapidly enlarging breast mass with skin involvement.[7] Owing to the small number of cases of lupus mastitis and breast malignancy in our cases, we did not observe any specific imaging features to distinguish between these two entities in our review. The concept of lupus panniculitis being exacerbated by localised trauma, such as biopsy, has been described.[8] However, due to the similarities of clinical presentation and imaging findings between lupus mastitis and breast malignancy, we advocate biopsy for histopathological correlation when suspicious imaging features are present.

The differential diagnosis of the findings seen in lupus mastitis include diabetic mastopathy, idiopathic granulomatous mastitis, and lymphoma. Clinical history is crucial in distinguishing diabetic mastopathy from lupus mastitis, while histopathological correlation to rule out idiopathic granulomatous mastitis (which lacks lymphocytic vasculitis), and immunohistological chemical staining for lymphoma may be needed to distinguish among these entities.

The clinical course of lupus mastitis is often chronic with flares and remissions.[6] Both patients with lupus mastitis had subjective breast mass during the follow-up periods while they also had mild flares of other clinical aspects of SLE. This suggests that the course of lupus mastitis may be associated with the overall disease course and process, though more research is needed to establish the potential association.

Breast Mass

Apart from lupus mastitis, breast masses that affect patients without lupus can also be present in patients with SLE. Probably benign (BI-RADS 3) oval circumscribed hypoechoic masses were the most frequently encountered imaging findings in our patient cohort, as these are also commonly seen in women without SLE. In our review, all of the cases either showed benign pathological results or were stable on imaging follow-up over the period of 3.5 to 7 years. These breast masses can be managed as per those in patients who are unaffected by SLE.

Previous literature has shown that SLE is associated with an increased risk of cancers overall, but is not more significantly associated with breast cancer.[15,16] Since the radiological features of lupus mastitis, tumour and other benign entities can overlap, as for patients unaffected by SLE, histological correlation is warranted when suspicious clinical and imaging features are present.

Calcifications

SLE causing lupus panniculitis is one of a few systemic diseases that can cause stromal calcifications of the breasts. Other systemic diseases which can cause diffuse dystrophic calcifications of the subcutaneous fat include scleroderma and dermatomyositis.[17] In lupus mastitis, thin curvilinear calcifications seen in the early phase of the disease progressively enlarge and coarsen to form dystrophic calcifications due to the evolution of fat necrosis as described earlier.

Other breast calcifications that are not lupus-related can also be present in patients in SLE, for example a suspicious group of fine pleomorphic microcalcifications in the case of invasive ductal carcinoma. Biopsy is warranted when suspicious microcalcifications are present, as for patients without SLE.

Vascular Manifestations

Arterial calcifications observed as tram-track calcifications on mammogram were present in three of our patients (Figure 8). Patients with SLE have been shown to have significantly higher prevalence and extent of systemic arterial calcifications compared with age- and sex-matched controls.[18] This is probably multifactorial in nature, as lupus-related renal disease, corticosteroid-induced dyslipoproteinaemia, and secondary hypertension from renal disease all contribute to accelerated atherosclerosis.[19] In our three cases with arterial calcifications, two of them did not have history of traditional risk factors for atherosclerosis, thus the arterial calcifications may be secondary consequence of SLE, given their known history of lupus nephritis. On mammography, arterial calcifications are regarded as incidental findings with no specific treatment indicated.

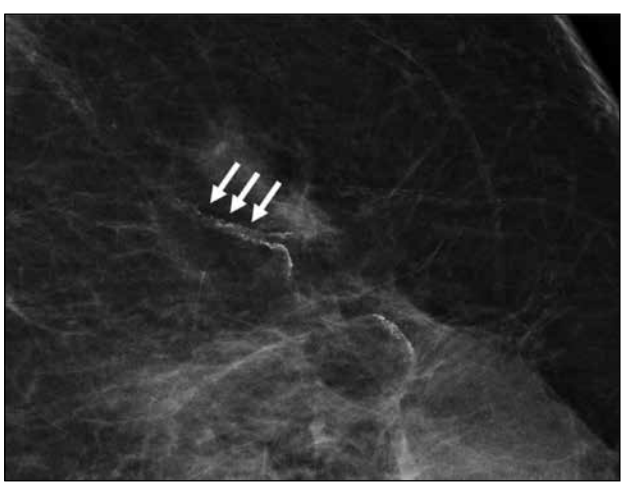

Figure 8. Mammogram showing tram-track calcifications compatible with arterial calcifications in a patient with systemic lupus erythematosus.

Mondor's disease is a rare entity characterised by thrombophlebitis of superficial veins, usually of the chest wall or breast.[20] Many possible aetiologies have been described, including trauma, local inflammation, malignancy, rheumatologic diseases including SLE, and hypercoagulable states, which can be also associated with SLE.[21] The presentation can be painful or painless, classically with sudden appearance of a subcutaneous cord. The course of the disease is benign and self-limiting, lasting between 4 to 8 weeks.[22] Mammography should be performed to exclude underlying malignancy, which is one of the potential causes of Mondor's disease.[23] On mammography, the thrombosed, inflamed vein is seen as a tubular density in the region of pain or a palpable mass, which may be mistaken for a dilated duct.[24] Ultrasound correlation is helpful, with findings including an enlarged superficial vessel with absent Doppler flow with or without intraluminal thrombus. A thrombosed vein tends to be longer than a duct and has a beaded appearance.[24]

Breast Oedema

On imaging, breast oedema is seen as breast enlargement, increased parenchymal density, trabecular thickening, increased interstitial markings, and skin thickening.[23,25] In patients with SLE, breast oedema can be secondary to lupus-related chronic renal failure or congestive heart failure, which usually affects both breasts but can be unilateral with lateralisation to the dependent breast in cases where patient is immobile. In patients with an upper limb arteriovenous fistula for dialysis, unilateral breast oedema can also occur secondary to complications of arteriovenous fistula such as thrombosis.[9] Occasionally, breast oedema can be associated with lupus mastitis, as in the case in our patient cohort (Figure 3). As with patients without SLE, breast oedema can also be caused by venous obstruction, inflammatory breast cancer, mastitis, post-irradiation changes, or lymphatic obstruction.

Axillary Lymphadenopathy

Many autoimmune diseases are associated with lymphadenopathy, including rheumatoid arthritis, Sjögren's syndrome and SLE. Lymphadenopathy has been reported to affect 23% to 34% of patients with SLE. Seven of our 16 patients (43.8%) were reported to have enlarged axillary lymph nodes, slightly higher

than the reported percentage. In general, lymph nodes related to SLE are soft, non-tender and vary in size and there may be fluctuation of lymphadenopathy with SLE disease exacerbations. Lymph node pathology in this case generally showed diffuse hyperplasia with scarce follicles.[26,27]

In patients with SLE, axillary lymphadenopathy can be due to the disease itself or occasionally related to lupus mastitis. SLE has been shown to be associated with an increased risk of non-Hodgkin lymphoma and Hodgkin lymphoma, which can also present with lymphadenopathy.[15] Other causes of axillary lymphadenopathy not related to SLE include metastasis (most commonly from breast cancer), infection, inflammatory causes, or granulomatous diseases.

On breast imaging, axillary lymph nodes are most commonly seen on the mediolateral oblique view mammogram or ultrasound. There can be considerable overlap in morphological appearances of benign and pathological lymph nodes on imaging. Features that are suspicious for pathological lymph nodes include loss of the normal fatty hilum, loss of the normal oval or reniform shape, poorly circumscribed margins, and increased size and opacity compared with findings on prior images.[9] It is important to not assume that nodal enlargement is reactive until malignancy has been ruled out, and pathological correlation is warranted if clinical suspicion is present.

In conclusion, our review showed a wide spectrum of breast manifestations and mostly nonspecific imaging findings that are primary or secondary to SLE. It is important for clinicians and radiologists to be aware of these SLE-related breast manifestations as they may have an impact on the management plan. No recognised imaging features distinguishing between lupus mastitis and breast malignancy have been identified, and pathological correlation is advocated in cases where suspicious imaging features are demonstrated.

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