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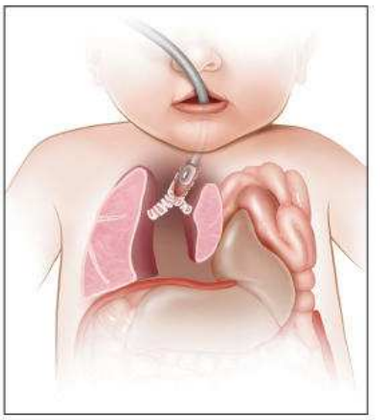

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Mimickers of Breast Malignancy on Breast Sonography

So Hyun Cho, MD, Sung Hee Park, MD

The aim of this article is to review benign breast lesions that can mimic carcinoma on sonography. Cases of benign lesions mimicking carcinoma on sonography were collected among lesions that were initially assessed as suspicious on sonography according to the American College of Radiology Breast Imaging Reporting and Data System category. Sonographically guided core needle biopsy was performed, and the pathologic types were confirmed to be benign. Cases of benign lesions mimicking carcinoma on sonography were shown to include fat necrosis, diabetic mastopathy, fibrocystic changes, sclerosing adenosis, ruptured inflammatory cysts, inflammatory abscesses, granulomatous mastitis, fibroadenomas, fibroadenomatous mastopathy, and apocrine metaplasia. Benign breast lesions may present with malignant features on imaging. A clear understanding of the range of appearances of benign breast lesions that mimic malignancy is important in radiologic-pathologic correlation to ensure that benign results are accepted when concordant with imaging and clinical features but, when discordant, there is no delay in further evaluation up to and including excisional biopsy.

Key Words—breast; mimickers; sonography

Benign breast lesions may present with malignant features on sonography. Imaging findings are used to classify breast lesions into the benign category 2, probably benign category 3, suspicious category 4 (A–C), and highly suspicious for malignancy category 5 according to the American College of Radiology Breast Imaging Reporting and Data System. Radiologists and clinicians must understand the spectrum of imaging features possible for breast lesions to establish an algorithm for treating patients. On sonography, the presence of circumscribed margins, an abrupt interface, and a homogeneous echo texture increase the probability that the lesion is benign. However, breast nodules often do not fulfill the strict criteria for benign or malignant lesions. Some benign lesions appear malignant on sonography due to an irregular shape, noncircumscribed margins (indistinct, angular, microlobulated, and spiculated), solid and cystic components, a nonparallel orientation, and posterior acoustic shadowing. Such lesions are initially determined to be suspicious, at which point sonographically guided core needle biopsies are performed. As in the cases described in this article, the pathologic type is often revealed to be benign after biopsy or surgical excision.

Benign lesions that can mimic breast carcinoma include atypical fibroadenomas, granulomatous mastitis, fat necrosis, papillomas, fibrocystic changes, sclerosing adenosis, fibrosis, and pseudoangiomatous stromal hyperplasia. These lesions may show a heterogeneous internal echo texture, microlobulations, an echogenic interface, and posterior shadowing, similar to breast carcinoma.

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Abbreviations
BI-RADS, Breast Imaging Reporting and Data System

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In this article, we present several mimickers of breast malignancies that were assessed as having a low suspicion or an intermediate concern for malignancy (category 4A or 4B) on initial imaging but then proved to be benign on sonographically guided core needle biopsies.

Fat Necrosis

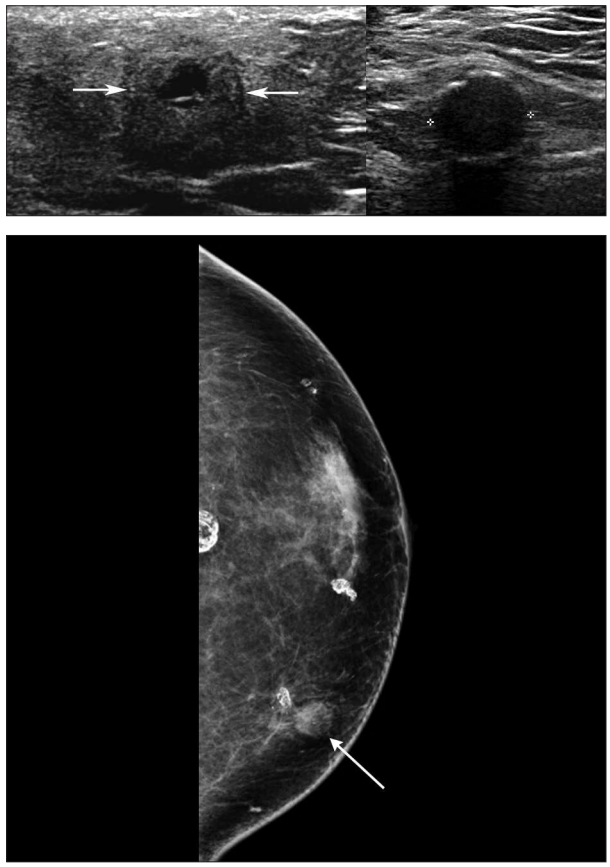
Fat necrosis of the breast is a common benign inflammatory process resulting from injury to breast fat. The pathogenesis of fat necrosis sheds light on the imaging features, which range from benign to malignant. Fat necrosis can cause palpable breast abnormalities that are often difficult to differentiate from breast carcinoma. It can result from accidental trauma, however, most cases are seen after surgery or radiation therapy.[1] Traumatic fat necrosis of the breast is a nonsuppurative inflammatory process, which results in variability of the imaging features. The lesions are characteristically situated near the skin or areolas because these are the sites within the breast that are most vulnerable to trauma.

Sonographic findings in fat necrosis vary with the different stages of the pathologic response to the fat necrosis.[2] Initially, there is a disruption of fat cells with hemorrhage and an inflammatory infiltrate. During the subsequent reparative phase, fibroblasts proliferate at the periphery of the lesion, and fibrosis eventually replaces necrotic fat.[3] Although masses caused by fat necrosis are usually solid on sonography, they can also appear complex with mural nodules or with echogenic bands, anechoic with posterior acoustic enhancement, anechoic with shadowing, or without a visible mass (Figure 1).[4,5] Mammographic findings of fat necrosis have been reported as oil cysts, round opacity, focal asymmetry, coarse dystrophic calcifications, clustered pleomorphic microcalcifications, and suspicious spiculated masses.[1,4,6] The mammographic findings reflect the amount of fibrosis. The reparative fibrotic reaction may replace all of the radiolucent necrotic fat, resulting in focal asymmetry or a focal mass (Figure 1, bottom).[7] Calcifications related to fat necrosis are usually round or curvilinear. However, they rarely may manifest as focal clustered pleomorphic microcalcifications that are indistinguishable from malignancy and that represent early-stage breast malignancy such as ductal carcinoma in situ. To diagnose fat necrosis without performing a biopsy, the patient's history should be evaluated for a history of trauma, surgery, or radiation therapy. Importantly, fat necrosis presents on sonography with increased echogenicity of the subcutaneous fat tissues. This appearance likely represents the sterile inflammatory process that defines fat necrosis histopathologically and is strongly suggestive of fat necrosis.[4] Fat necrosis shows characteristic mammographic findings, and these are more specific than sonographic findings.[6] Therefore, the combination of sonographic and mammographic findings allows the correct diagnosis of fat necrosis and can avoid unnecessary biopsy.

Diabetic Mastopathy

Diabetic mastopathy is a variant of stromal fibrosis that occurs in patients with diabetes. The pathogenesis is likely multifactorial. Prolonged hyperglycemia may alter the

Figure 1. Images from a 58-year-old woman with a palpable lesion in her left breast. Top left, Lower medial sonogram showing a complex cystic mass (arrows) with surrounding edematous fat of mixed hyperechogenicity and hypoechogenicity in the left breast. Within the internal cystic mass, thin echogenic lines are visible. This mass was confirmed on pathologic examination to be fat necrosis after a sonographically guided 14-gauge core needle biopsy. Bottom, On mammography, the mass manifested as round opacity in the left lower inner portion (arrow). Top right, After 18 months, the wall of the nodule calcified, focal cystic changes within the nodule disappeared, and intense posterior shadowing was noted.



formation of nonenzymatic glycosylated end products and neoantigens, or it may lead to B-cell–predominant inflammation with an autoimmune response, both of which would lead to an abnormal immune reaction in which there is an abnormal accumulation of extracellular matrix.[8] This reaction results in extracellular matrix expansion secondary to increased collagen production and decreased degradation.[9] Diabetic mastopathy presents clinically as a hard mass. The most common symptom is a palpable, very firm, nontender mass or thickening of the skin. On average, there is a 20-year interval between the onset of diabetes and the development of a palpable mass.

Sonography is the most useful diagnostic tool for evaluating a palpable mass in a patient suspected of having diabetic mastopathy. Fine-needle aspiration is often nondiagnostic because of insufficient cellular material secondary to extensive fibrosis.[9] The typical sonographic findings in diabetic mastopathy are the presence of marked posterior acoustic shadowing with an associated poorly defined heterogeneous hypoechoic mass (Figure 2). An atypical presentation with a well-circumscribed nodule has also been reported.[10] Generally, no vascularity is visible on color Doppler imaging. These masses consist primarily of fibrous tissue, which causes strong acoustic shadowing.[10] The imaging findings of diabetic mastopathy may be confused with breast cancer. The differential diagnosis includes carcinoma and focal or stromal fibrosis. Although it is widely reported in the literature that diabetic mastopathy is neither premalignant nor malignant, patients should be routinely followed with magnetic resonance imaging or sonography and core biopsy if the lesions become clinically or radiologically suspicious for malignancy.[11] The recognition of diabetic mastopathy requires an awareness that this entity exists and a careful correlation of the patient's clinical history with the physical, radiologic, and pathologic characteristics of the breast lesion.

Fibrocystic Changes

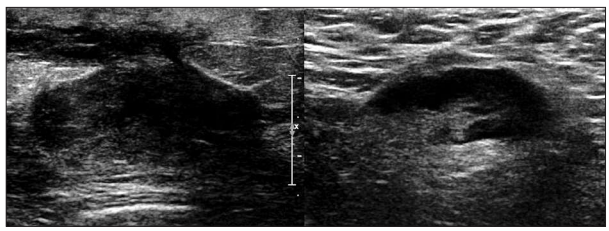
Fibrocystic changes constitute a clinical diagnosis but on histopathologic examination consist of a constellation of cysts, fibrosis, and adenosis. This condition is benign and considered a normal variant. The most common symptoms are mastalgia, particularly in the outer portion of the breasts. Fibrocystic changes can be categorized into 2 subgroups by histopathologic features: nonproliferative and proliferative.[12] Whereas nonproliferative lesions have no evidence of an increased cancer risk, proliferative lesions can contain atypical ductal or lobular hyperplasia and do represent a risk of breast cancer.[13] Fibrocystic changes may appear focal, regional, or diffuse. In postmenopausal woman receiving hormone replacement therapy, especially estrogen therapy, the cystic component of fibrocystic changes will increase. Sonographic findings in fibrocystic changes can be scattered echogenic foci due to calcifications, simple cysts, complicated cysts, clustered cysts, and clustered microcysts. Fibrocystic changes can also present as complex cystic and solid masses or as discrete masses with irregular shadowing,[14] which are often difficult to distinguish from malignancies and require biopsy (Figure 3).

Sclerosing Adenosis

Sclerosing adenosis is a proliferative lesion that is most common in perimenopausal women. It is present in 12% of benign and 5% to 7% of malignant specimens on histopathologic examination.[15,16] In particular, sclerosing adenosis may have some features that resemble breast malignancy clinically and radiographically. Physical examination may reveal a firm mass or multiple firm palpable masses with indistinct margins.[17] Sclerosing adenosis has a wide spectrum of radiologic appearances. It can manifest as a suspicious finding on mammography, such as architectural distortion or indeterminate microcalcifications.[18] The most frequent microcalcification patterns are amorphous or pleomorphic clustered and scattered microcalcifications.[16,18,19] In a previous study,[19] the most frequent lesions were masses, and 80% of the masses had irregular contours.[19]

A previous study[20] reported sonographic findings of pathologically proven nodular adenosis. All of the nodules were hypoechoic and circumscribed, and most of the lesions were oval with posterior acoustic enhancement. However, the typical sonographic appearance of nodular sclerosing adenosis is nonspecific and nonpathognomonic (Figure 4). Furthermore, it can present with a contrast

Figure 2. Images from a 47-year-old woman with a palpable mass and skin thickening in her right breast. Left, Sonogram showing skin thickening and a hypoechoic mass with partially indistinct margins extending in the subareolar region with posterior shadowing. Right, There were also enlarged lymph nodes measuring 1.5-cm with cortical thickening in the ipsilateral axilla. The mass was assessed as BI-RADS category 4A, and a sonographically guided core needle biopsy was performed. Pathologic findings confirmed diabetic mastopathy.



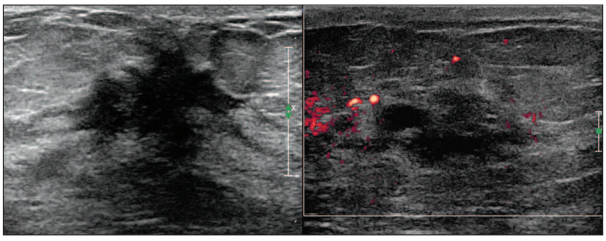


Figure 3. Images from a 54-year-old woman who underwent breast screening sonography. Left, There was an irregularly shaped spiculated hypoechoic mass with microlobulated margins in the left upper outer quadrant. Right, There was focal increased vascularity in the surrounding breast tissue. The lesion was assessed as BI-RADS category 4B (intermediate concern for malignancy); thus, a sonographically guided 14-gauge core needle biopsy was performed, and pathologic examination confirmed fibrocystic changes.

enhancement pattern similar to that of a malignant process on breast magnetic resonance imaging.[17] A biopsy is needed to differentiate sclerosing adenosis from other benign lesions and from malignancy. However, a pathologic diagnosis may be challenging even on histologic examination. Although the cytologic features obtained from fine-needle aspiration specimens correlate closely with the histologic appearance, the features are nonspecific and therefore are not prospectively diagnostic of sclerosing adenosis. Core needle biopsy is generally a reliable sampling method for establishing the diagnosis of sclerosing adenosis. The main diagnosis in the differentiation of sclerosing adenosis is low-grade breast carcinoma, such as tubular carcinoma.[21] In some cases, sclerosing adenosis may involve in situ or invasive carcinoma, and some studies have reported cases that were diagnosed as sclerosing adenosis on core needle biopsy but were later proven malignant on excisional biopsy.[20,22] Sclerosing adenosis may show radiologic and pathologic features that overlap with those of breast carcinoma. If the pathologic features are atypical and not consistent with a benign lesion, or if the radiologic findings are suspicious for malignancy, rebiopsy or surgical resection should be advised.

Ruptured Inflammatory Cysts

Histopathologically, this diagnosis consists of inflammatory cells surrounding a cyst wall and cyst contents. On sonography, ruptured cysts present as a thick-walled cystic masses or complex cystic masses containing anechoic fluid or echogenic debris (Figure 5). The most common finding is a cystic lesion with indistinct margins.[23] These findings are due to the leakage of irritating cyst contents, which incite an inflammatory response. The cyst may also contain a fluid-debris level with debris adherent to the lesion wall, mimicking an intracystic mass. However, the sonographic appearance is nonspecific and often requires aspiration or biopsy. On magnetic resonance imaging, a ruptured inflammatory cyst presents as a cyst with a thin rim of enhancement.[24] When the lesion appears as a thick-walled cyst or complex cystic lesion, core needle biopsy is needed. During the core needle biopsy procedure, the lesion usually ruptures so that it disappears or is markedly decreased in size on follow-up.

Inflammation With Abscesses

Breast abscesses develop as a complication of mastitis. They are classified into 2 categories: lactational (puerperal) and nonlactational (periductal). Puerperal mastitis is associated with pregnancy or lactation, reproductive

Figure 4. Images from a 43-year-old woman with breast pain who underwent breast sonography. Left, Sonogram showing an irregularly shaped microlobulated hypoechoic nodule in the left breast. Right, There was no vascularity in the nodule. The nodule was assessed as BI-RADS category 4A (low suspicion), and a sonographically guided core needle biopsy was performed. Pathologic findings confirmed sclerosing adenosis.

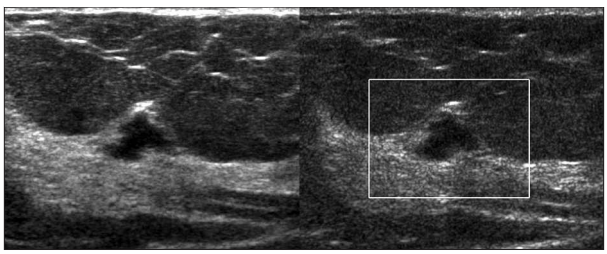
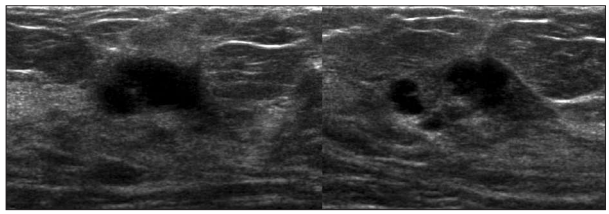


Figure 5. Images from a 42-year-old woman with palpable lesions in the right breast. Left, Sonogram showing an irregularly shaped cystic lesion. Right, There were internal echoes and an echogenic interface. After a sonographically guided biopsy was performed, pathologic findings confirmed a ruptured inflammatory cyst.



maternal age, and in 5% to 10% of women in their puerperal period. Pathogens are transmitted to the breast from infants or a cracked nipple. Milk stasis causes duct dilatation and disruption. Lipids in periductal tissue incite inflammation. Periductal mastitis usually affects nonlactating women in their perimenopausal years. Smoking and nipple rings are independent risk factors.[25] The overall incidence of smoking is about 30% to 60% in women with periductal mastitis. Smoking may damage the subareolar ductal epithelium by its direct effect of toxic metabolism.[25–27] Periductal mastitis often is regarded as a secretary disease that is a response to irritative contents of intraluminal lipids. Extravasation of lipid contents from obstructed ducts into adjacent tissues causes an inflammatory reaction. Plasma cells accumulate in the periductal stroma. Periductal mastitis in teens and those in their 20s is often associated with congenital nipple inversion. Diagnosis of breast abscesses can easily be made on the basis of the clinical presentation of inflammation, including local heat, swelling, pain, redness of the overlying skin, and, occasionally, signs of systemic infection. However, the presentation in some patients may mimic malignancy both clinically and radiologically.

The typical sonographic features of inflammation with abscesses are hypoechoic lesions containing low- or medium-level internal echoes that represent necrotic debris with an irregular shape and relatively poorly defined margins (Figures 6 and 7). In the acute phase of inflammatory mastitis, sonography shows decreased parenchymal echogenicity due to edema, dilated and thickened ducts, and skin thickening; an acute abscess can be appreciated only by depiction of a poorly defined anechoic or hypoechoic fluid-filled space containing a few irregularly distributed internal echoes (Figure 8).[28] One study reported 2 points to differentiate between a breast abscess and malignancy: about one-third of patients with breast abscesses had adjacent interstitial fluid and a hypoechoic wall, whereas no patients with breast cancer had these findings.[29] These findings are usually assessed as having a low suspicion or suspicious according to the BI-RADS classification. However, core needle biopsy is required for definite diagnosis.

Granulomatous Mastitis

Idiopathic granulomatous mastitis is a rare benign breast disease characterized by chronic necrotizing granulomatous lobulitis. Although the etiology of granulomatous mastitis remains unclear, an autoimmune reaction is favored. This disease typically affects younger women with a recent history of pregnancy and lactation. Wide local excision, with or without corticosteroid therapy, has been associated with a lower rate of recurrence and lower complication rates.[30] For complicated and resistant cases, steroids should be administered after excision. Idiopathic granulomatous mastitis often mimics breast carcinoma

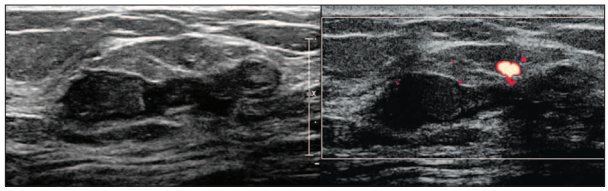


Figure 6. Images from a 44-year-old woman with a history of right mastectomy who underwent sonography for a palpable lesion in her left breast. Left and Right, Sonograms showing an elongated cystic and solid hypoechoic mass in her left breast. Considering her cancer history, this lesion was assessed as BI-RADS category 4B (intermediate concern for malignancy). A sonographically guided 14-gauge core needle biopsy was performed, and pathologic findings confirmed chronic inflammation.

Figure 7. Images from a 46-year-old woman with a palpable breast mass. Left, On sonography, the lesion had a thick wall, lobulated margins, an echogenic interface, and a complex internal echo pattern. This complex cystic lesion was assessed as BI-RADS category 4B (intermediate concern for malignancy). Right, There was no vascularity in the nodule. A sonographically guided core needle biopsy was performed, and pathologic findings confirmed chronic inflammation.

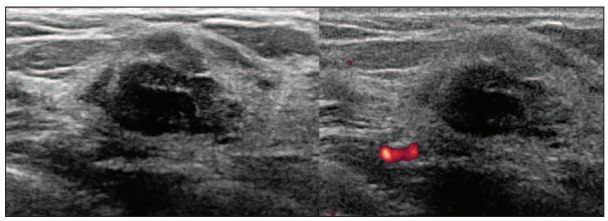
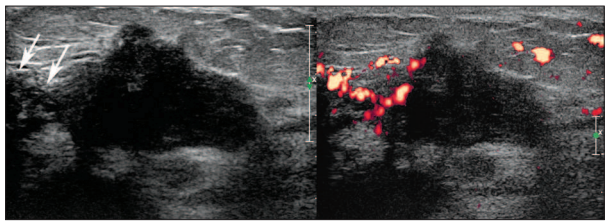


Figure 8. Images from a 36-year-old woman with pain and a palpable mass in her right breast. Left, Sonogram showing an irregularly shaped hypoechoic mass that was poorly defined in some areas and extended into the periareolar ducts (arrows). Right, Surrounding tissue showed increased echogenicity due to edema with hypervascularity. Pathologic findings after a core needle biopsy confirmed acute inflammation.



both clinically and radiologically, and the initial diagnosis often favors breast cancer.

Mammographic features are variable, ranging from normal to a mass with benign or suspicious features and focal asymmetric density, with the latter being the most frequently described abnormality.[30,31] The most common sonographic appearance is that of a discrete but irregular hypoechoic mass. However, multiple hypoechoic masses, parenchymal heterogeneity, and areas of heterogeneous echogenicity with parenchymal deformities have all been described.[32] The sonographic appearance of multiple, clustered, and often contiguous fingerlike hypoechoic tubular lesions is suggestive of the disease (Figure 9). These sonographic findings are also common in breast cancer. Usually, this disease entity is assessed as BI-RADS category 4. Granulomatous mastitis is a diagnosis of exclusion. Pathologic analysis shows a noncaseating, nonvasculitic granulomatous inflammatory reaction centered around the breast lobules.[33]

Fibroadenomas

Fibroadenomas are benign fibroepithelial tumors with mixed stromal and epithelial elements. The most common presentation of a fibroadenoma is a mobile solid mass in a woman younger than 35 years. Fibroadenomas grow anywhere in the breast parenchyma, show hormone-sensitive growth and involution, and typically present as highly mobile, palpable, painless, and firm masses. Most fibroadenomas are self-limited and involute spontaneously. They have been noted to develop with chronic cyclosporine A therapy after renal transplantation.

On sonography, fibroadenomas present as circumscribed oval or gently lobulated hypoechoic or isoechoic masses with homogeneous low internal echogenicity. Between 2% and 4% of fibroadenomas contain echogenic foci associated with calcifications. Fibroadenomas show variable posterior enhancement. On color Doppler imaging, there are often visible peripheral feeding vessels. Growth greater than 20% in diameter in 6 months suggests a phylloides tumor, at which point surgical excision is recommended. Twenty-five percent of fibroadenomas show irregular margins, and 10% have intratumoral calcifications.[34,35] These findings are suspicious; therefore, the lesions are usually assessed as suspicious with a BI-RADS category of 4 (Figure 10).

Fibroadenomatoid Mastopathy

Fibroadenomatous mastopathy is a benign proliferative lesion. Pathologically, it is an intermediate step or is arrested at an intermediate step during the histogenesis of fibroadenomas. The pathologic characteristics of fibroadenomatous mastopathy differ from those of fibroadenomas in that the stromal hyperplasia may not have well-defined borders and usually involves several lobules.[36] On sonography, fibroadenomatous mastopathy appears as a circumscribed lobulated mass with heterogeneous echogenicity and internal echogenic septations (Figure 11). Despite the well-circumscribed margins, the lesions are suspicious considering the possibility of well-circumscribed breast cancer or metastatic lymph nodes.[37] The imaging findings of fibroadenomatoid mastopathy are not sufficiently characteristic to distinguish the lesion from a fibroadenoma or well-circumscribed carcinoma. Biopsy is necessary to differentiate this lesion from other benign and malignant tumors. A core needle biopsy of this lesion may prove to be diagnostic.

Figure 9. Images from a 32-year-old woman with nipple discharge. Left, Sonogram showing a poorly defined hypoechoic mass with tubular tracks to the periareolar area (arrows). Edema is visible as surrounding increased echogenicity. Right, Focal increased vascularity was noted at the peripheral portion of the lesion. The pathologic interpretation after core needle biopsy was granulomatous mastitis.

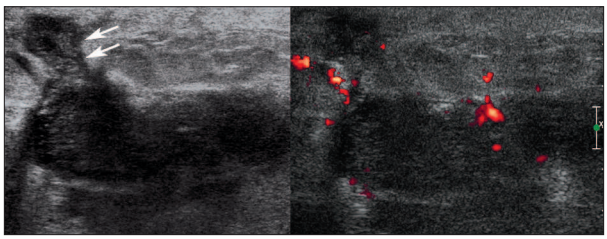
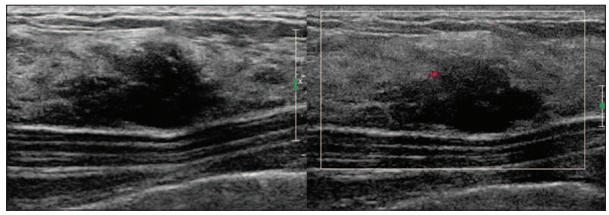


Figure 10. Images from a 25-year-old woman with a painful lump in the right breast. There was a 2-cm hypoechoic mass in her right upper outer breast. Left, The mass had microlobulated margins and a markedly hypoechoic heterogeneous internal echo pattern. Right, There was no increased vascularity. This mass was assessed as BI-RADS category 4A (low suspicion). Pathology findings after a 14-gauge core needle biopsy confirmed fibroadenoma.



Apocrine Metaplasia

Apocrine metaplasia refers to pathologically dilated acini lined by columnar-type secretary epithelium with a granular, eosinophilic cytoplasm. Apocrine metaplasia is often associated with fibrocystic changes. It is not premalignant, but atypical apocrine metaplasia is associated with a 5.5-fold increased relative risk of cancer.[38,39] The lesion usually presents on sonography as an incidental new or enlarging microlobulated mass or clustered microcysts. The best diagnostic clue can be the clustered microcysts on sonography, especially if there is an indistinct border. However, this common finding overlaps with fibrocystic changes. Other sonographic findings include complex microcysts and microcysts with milk of calcium.[23,40]

Mammography typically shows smooth well-defined masses with microlobulated or macrolobulated margins. This lobulation correlates with the typical sonographic appearance of multiple anechoic spaces, suggesting apocrine metaplasia.[39] However, apocrine metaplasia can also present as thick-walled cysts or as a complex cystic lesion (Figure 12) and needs short-term follow-up or biopsy.

Figure 11. Images from a 54-year-old woman with a palpable mass in her left upper outer breast near the axilla. Left, Sonogram showing a well-circumscribed hypoechoic mass with a heterogeneous internal echo texture. Right, There was increased vascularity. The lesion was assessed as BI-RADS category 4B (intermediate concern for malignancy) due to the heterogeneous internal echo texture and the possibility of a well-circumscribed breast malignancy or lymph node metastasis. A sonographically guided core needle biopsy showed fibroadenomatous mastopathy.

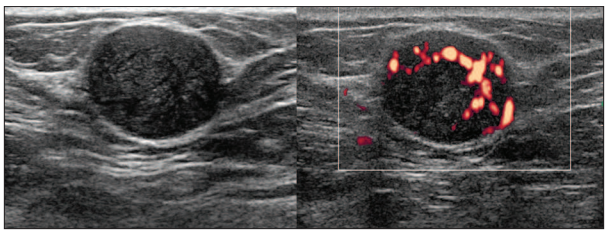
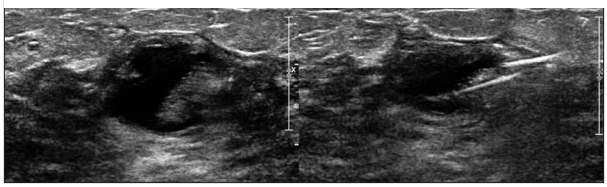


Figure 12. Images from a 43-year-old woman with a surgical history of rectal cancer with a new palpable right breast mass. Left, Sonogram showing a complex solid and cystic mass with an irregularly thickened wall. Right, A sonographically guided core needle biopsy targeted the solid portion. Pathologic findings confirmed apocrine metaplasia.



Biopsy is needed if the lesion is rapidly enlarging or if there is a solid component within the cystic lesion.

Conclusions

This article has aimed to provide a pictorial review of the imaging findings of benign breast lesions that mimic malignancy. We reviewed the sonographic findings of fat necrosis, diabetic mastopathy, fibrocystic changes, sclerosing adenosis, ruptured inflammatory cysts, inflammation with abscesses, granulomatous mastitis, fibroadenomas, fibroadenomatous mastopathy, and apocrine metaplasia. Benign breast lesions sometimes present with malignant features on imaging. Radiologists should be familiar with the imaging features of these lesions to plan an appropriate diagnostic approach.

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