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BREAST IMAGING

PICTORIAL ESSAY

Radiologic and histopathologic review of rare benign and malignant breast diseases

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ABSTRACT

High social awareness of breast diseases and the rise in breast imaging facilities have led to an increase in the detection of even rare benign and malignant breast lesions. Breast lesions are associated with a broad spectrum of imaging characteristics, and each radiologic imaging technique reflects different characteristics of them. We aimed to increase familiarity of the radiologist with these uncommon lesions as well as correlate histopathologic findings with the radiologic imaging features of the tumors. Histopathologic examination is necessary in the evaluation of such breast lesions, particularly when radiologic images are not definitive for a specific diagnosis.

High social awareness of breast diseases and the rise in breast imaging facilities have led to an increase in detection of some rare benign and malignant breast lesions. Radiologists have been compelled to overcome the issue of uncommon and challenging breast lesions. These rare breast lesions are fibromatosis, idiopathic granulomatous mastitis, tubular adenoma, diabetic mastopathy, invasive micropapillary carcinoma, osteoclastic giant cell breast carcinoma, malignant phyllodes tumor, carcinoma arising in fibroadenoma, metastasis, and metaplastic carcinoma. Imaging findings of these lesions are usually nonspecific, and pathologic examination is required for diagnosis. These tumors could be detected by self or clinical examination or by radiologic screening, and they are associated with broad imaging characteristics. Different imaging modalities may reflect different characteristics of them.

We aimed to increase the familiarity of the radiologist with these uncommon breast lesions and to correlate their radiologic and histopathologic findings.

Uncommon benign lesions of the breast

Fibromatosis (Desmoid tumor)

Fibromatosis is characterized by a localized infiltrating mass that contains fibroblasts and collagen (1). Generally, it manifests as a single, palpable, nontender mass and is sometimes fixed to the fascia beneath. Skin retractions may mimic breast cancer. Fibromatosis of the breast is extremely rare, constituting less than 0.2% of all breast tumors (2). It develops from aponeurotic fascia of pectoral muscle or from breast tissue (3). Gardner syndrome, silicone implants, or surgical scars might induce these lesions. They are usually seen in reproductive ages and are associated with elevated estrogen levels. These lesions appear as irregular hypoechoic masses with posterior shadowing that resemble malignancy on ultrasonography (US) and as dense noncalcified masses with irregular margins on mammography. On dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) lesions are hypo- or isointense on T1-weighted imaging and heterogeneous hyperintense on T2-weighted imaging, without strict margins and show slow wash-in pattern. They also might have rapid enhancement with type II (plateau) or type III (wash-out) curves consistent with a malignant lesion. The mass might extend through chest wall (4, 5). In some cases, lesions may display atypical ultrasonographic findings such as heterogeneous hyperechoic mass with an indistinct margin or heterogeneous echoic mass with internal anechoic area that may mimic malignancy or abscess

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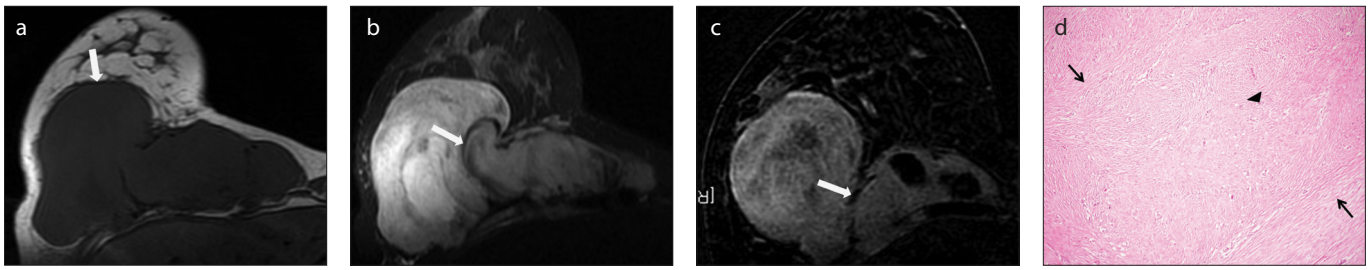

Figure 1. a–d. Fibromatosis (desmoid tumor). Axial T1-weighted image **(a)** shows a giant, circumscribed solid mass *(arrow)*. Axial T2-weighted **(b)** and subtraction **(c)** images reveal linear-curling, hypointense and nonenhancing internal septations within lesion *(arrow)*. Subtraction image **(c)** shows marked heterogeneous enhancement. Histopathologic examination **(d)** (hematoxylin eosin staining [H-E], ×40) demonstrates spindle cells containing collagen *(arrows)* and low rate of mitosis *(arrowhead)* constituting so-called "herringbone" pattern.

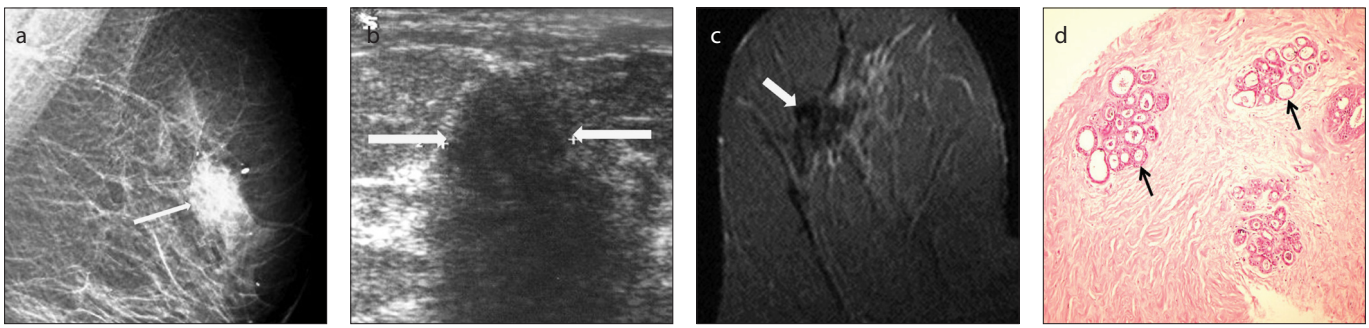

Figure 2. a–d. Focal fibrosis of the breast. Left mediolateral oblique (MLO) projection of mammography **(a)** shows a high density, irregular mass lesion *(arrow)* with indistinct margin. Axial grey-scale US image **(b)** shows an oval, hypoechoic, nonparallel solid lesion with indistinct margin and marked posterior acoustic shadowing *(arrows)*. Axial T2-weighted short tau inversion recovery (STIR) image **(c)** shows an oval lesion *(arrow)* with irregular margin; it is hypointense compared with the fibroglandular tissue. The lesion showed homogeneous mild enhancement on contrast enhanced series (not shown). The lesion was categorized as BI-RADS category 4b. Histopathologic examination **(d)** (H-E, ×40) demonstrates small lobules consisting of acinar structures within hyalinized stroma *(arrows)*.

(6, 7). These lesions consist of spindle cell fascicles and collagen at histopathologic examination.

In case of significant mitotic activity, along with low-to-intermediate cellularity, the diagnosis should be shifted to fibrosarcoma, which should be differentiated from benign lesions due to the risk of distant metastasis. Although fibromatosis recurs locally, it does not metastasize. Other benign entities, reactive scars, and fibromatosis-like metaplastic spindle cell tumor could be distinguished histologically (3). Fig. 1 shows a fibromatosis lesion in a 31-year-old woman.

Main points

- Fibromatosis (desmoid tumor) is a localized tumor that can be inflitrative and locally reccurent. It manifests as a single, palpable, nontender mass that is sometimes fixed to the fascia beneath.
- Tubular adenoma of breast is a rare benign tumor, which accounts for 0.13%–1.7% of breast lesions.
- Diabetic mastopathy term defines proliferation of mammarian fibrous tissue as a result of resistance to degradation of collagen in diabetic population.
- Malignant phyllodes tumor (previously known as cystosarcoma phyllodes or periductal stromal tumor) is a lobulated and well demarcated solid tumor with homogeneous or heterogeneous echotexture.

Focal fibrosis of the breast

Focal stromal proliferation associated with atrophy or hypoplasia of acini and ducts is termed as focal fibrosis of the breast. Synonyms of this entity are "focal fibrous disease of the breast," "fibrosis of the breast," "fibrous mastopathy," "fibrous tumor of the breast," and "focal fibrosis of the breast." Etiology remains unclear; however, fibroblastic proliferation triggered by estrogen is suggested in the literature (3). Nonpalpable lesions may be detected incidentally by US or mammography, while a certain subgroup of patients present with a palpable mass (3). Focal fibrosis of the breast is common in premenopausal women. Mammographic features of lesions are; ovoid mass (51%), asymmetric density (49%), calcification (9%), lobular mass (6%), and irregular mass (4%), which are usually categorized as breast imaging reporting and data system 4 (BI-RADS 4) lesions (8). Rarely posterior shadowing is detected on US images. On DCE-MRI, they show plateau or wash-out curve after rapid or medium upslope.

Due to the widespread use of screening mammography and imaging-guided core biopsy, incidence of these lesions is on the rise (3). Prevalence of the disease among imaging-guided core biopsies is estimated as 2.1%–7.9% (3). Re-biopsies may be required because they mimic malignant lesions. Fig. 2 shows focal fibrosis in a 56-year-old woman.

Idiopathic granulomatous mastitis

Idiopathic granulomatous mastitis (IGM) is defined as granulomatous inflammation of breast lobules caused by unknown etiology (3). Breast feeding and oral contraceptive agents may be responsible in some cases (9). It is a rare entity and mostly affects parous women (9). IGM occurs mostly 2–6 years after pregnancy in women aged 22–42 years (9); rarely, older women may also suffer from IGM. Patients present with symptoms mimicking breast cancer such as hard lump, nipple retraction, and sinus formation. Mammography and US are usually used to rule out malignancy. Mammography depicts multiple small masses, asymmetric noncalcified densities or spiculation.

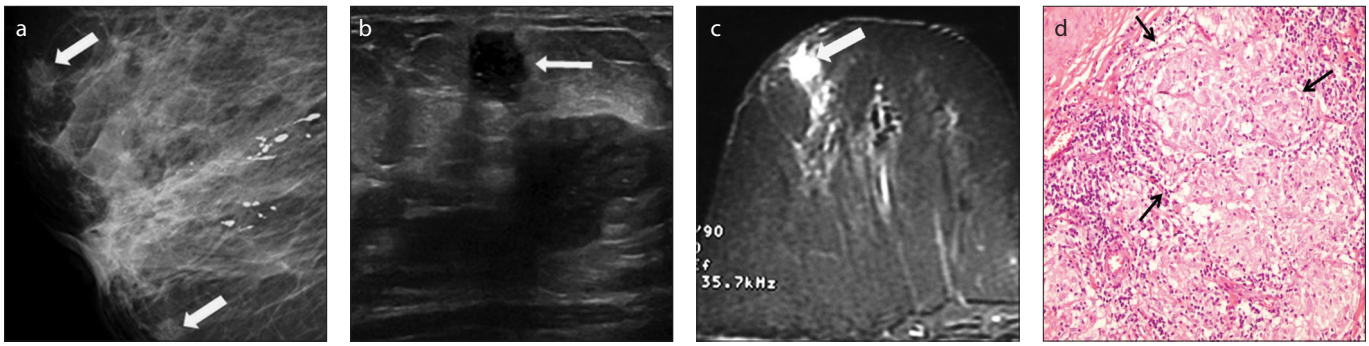

Figure 3. a–d. Idiopathic granulomatous mastitis. Right MLO projection of mammography **(a)** shows two round and equal density lesions with indistinct margins *(arrows)* in the premammarian area. Axial grey-scale US image **(b)** shows a round, microlobulated, nonparallel, and hypoechoic solid lesion surrounded by a hyperechoic halo *(arrow)*. T2-weighted STIR image **(c)** reveals multiple round lesions, with irregular margin *(arrow)*. The lesion was categorized as BI-RADS category 4a. Histopathologic examination **(d)** (H-E, ×40) demonstrates granulomas *(arrows)* without necrosis adjacent to ductules that are characteristic findings of granulomatous mastitis.

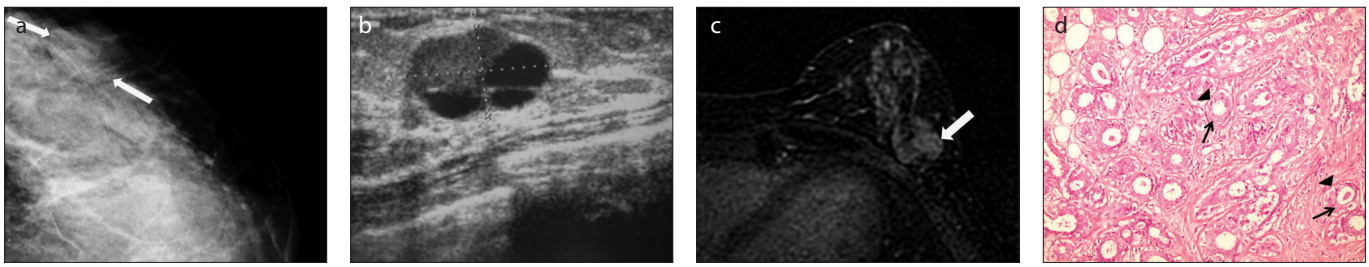

Figure 4. a–d. Tubular adenoma. Left craniocaudal projection of mammography **(a)** shows an oval, circumscribed, equal density mass *(arrow)* with peripheral lucent halo. Axial grey-scale US image **(b)** shows an oval, parallel, circumscribed, complex cystic and solid mass lesion with mild posterior acoustic enhancement. Subtraction image **(c)** reveals an oval, irregular lesion displaying slightly heterogeneous enhancement *(arrow)*. The lesion demonstrated persistent kinetic and was categorized as BI-RADS category 4a. Histopathologic examination **(d)** (H-E, ×40) demonstrates proliferation of double stratified epithelial *(arrows)* and myoepithelial cells *(arrowheads)* lining tubular structures.

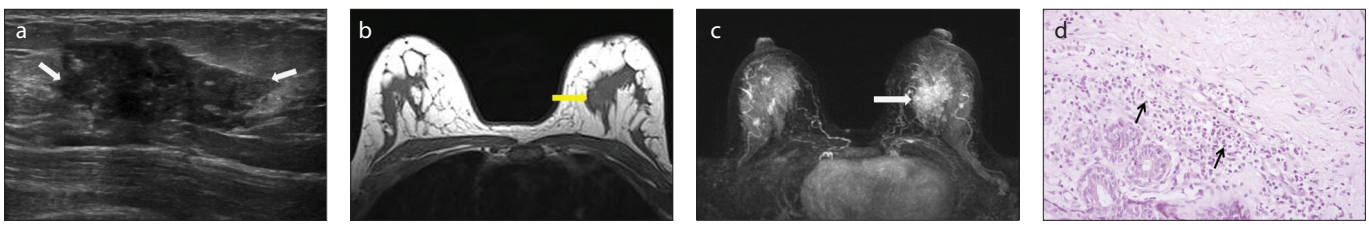

Figure 5. a–d. Diabetic mastopathy. Axial grey-scale US image **(a)** shows an irregular, parallel, heterogeneous lesion *(arrows)*. Axial T1-weighted image **(b)** shows an irregular lesion with irregular margin *(arrow)*. Maximum intensity projection image **(c)** reveals heterogeneous, regional enhancement *(arrow)* The lesion demonstrated type II kinetic (not shown). The lesion was categorized as BI-RADS category 4c. Histopathologic examination **(d)** (H-E, ×40) demonstrates perivascular lymphocytic infiltration *(arrows)* associated with atrophic lobules within areas of stromal fibrosis.

US shows clusters of tubular hypoechoic lesions or sometimes a solitary mass (10, 11). On MRI irregular masses or nonmass enhancement accompanied with microabscesses may be seen; MRI has an incremental value for the assessment of breast involvement and for monitoring treatment response (12). Other etiologies of granulomatous diseases such as tuberculosis, histoplasmosis, cysticercosis, sarcoidosis, autoimmune disease (poliangiitis granulomatosis, polyarteritis nodosa) should be excluded for definite diagnosis. Accurate diagnosis can only be made through histopathologic assessment. Histologic examination reveals inflammation in breast lobules and noncaseating granulomas containing clustered epitheloid histiocytes, lymphocytes, plasma cells, neutrophils, and giant cells (3). Fig. 3 shows an IGM in a 38-year-old woman.

Tubular adenoma

Tubular adenoma of the breast is a rare benign tumor which accounts for 0.13%–1.7% of breast lesions (13). Tubular adenomas are pure adenomas; they belong to an uncommon subtype of fibroadenoma (pericanalicular variant) often seen in young women. Grossly, they are well circumscribed lesions (14). Histologically, similar to florid adenosis, tubular adenomas consist of similar sized tubular structures showing epithelial proliferation. They differ from fibroadenomas by having scanty connective tissue and more acinar units instead of large ducts with epithelial component (14).

Differential diagnosis of tubular adenomas includes malignancy and noncalcified fibroadenoma. However, it is usually impossible to have a definitive radiologic diagnosis (14). Fig. 4 shows a tubular adenoma in a 45-year-old woman.

Diabetic mastopathy

Diabetic mastopathy term defines proliferation of fibrous breast tissue as a result of resistance to degradation of collagen in

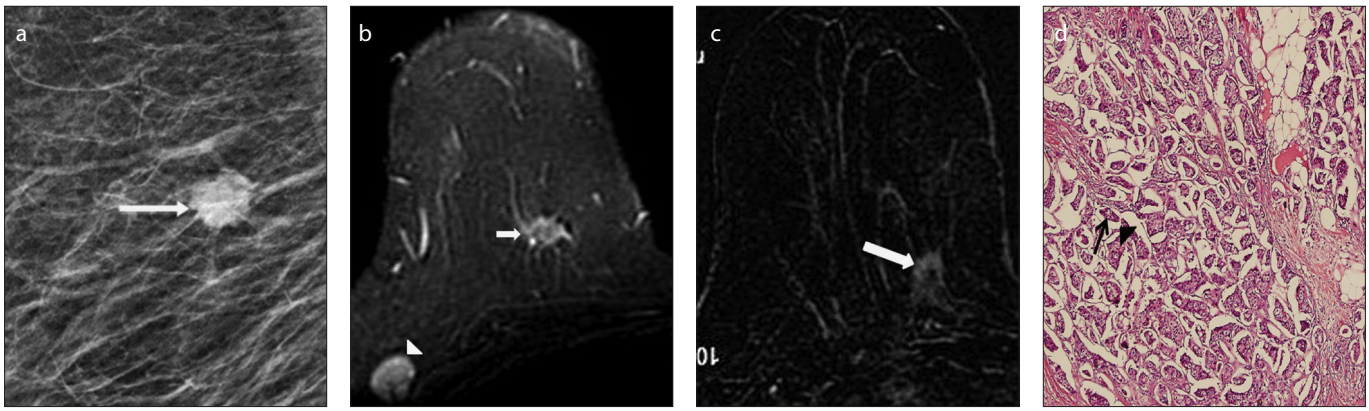

Figure 6. a–d. Invasive micropapillary carcinoma. Right MLO projection of mammography **(a)** shows an irregular, high-density spiculated mass *(arrow)*. Axial T2-weighted STIR image **(b)** shows a round, spiculated, heterogeneous hyperintense lesion *(arrow)* with ipsilateral axillary lymphadenopathy *(arrowhead)*. Subtraction image **(c)** reveals heterogeneous enhancement *(arrow)*. The lesion demonstrated wash-out kinetic (not shown). The lesion was categorized as BI-RADS category 5. Histopathologic examination **(d)** (H-E, ×100) demonstrates pathognomonic pseudopapillary structures *(arrow)* within lacunae *(arrowhead)*.

diabetic population. It is an uncommon fibrous proliferation that mimics tumors. It affects mostly premenopausal women (age range, 32.2–62 years) with a long history of type 1 diabetes (diabetes duration, 4–43 years) (15). Subjects present with single or multiple palpable, nontender, firm or hard masses in one or both breasts. Lesions do not reveal specific radiologic appearance. The common mammographic findings are ill-defined masses or asymmetric densities. These lesions are often masked by dense glandular tissue, which makes mammographic evaluation difficult. Significant posterior shadowing of lesions is the main US finding. It has been proposed that on MRI diabetic mastopathy may present as an enhancing mass and specific parenchymal contrast enhancement, which may help to differentiate it from carcinoma (16, 17). Histopathologically, they are seen as firm, homogeneous masses characterized by marked fibrosis and lymphocytic infiltration, which are localized in periductal, perivascular, and perilobar areas. Other characteristics are lobular atrophy and accumulation of epitheloid myofibroblasts (15). Fig. 5 shows diabetic mastopathy in a 47-year-old woman.

Uncommon malignant lesions of the breast

Invasive micropapillary carcinoma

Invasive micropapillary carcinoma (IMC) of the breast is considered as a rare subtype of infiltrating ductal carcinoma. IMC has been found to be associated with a high rate of axillary metastasis (about 75% at the time of diagnosis) and worse prognosis. The median diameter of tumor is 2.8 cm (range, 0.7–10 cm). Histopathologic signs typically include pseudopapillary structures with fibrovascular core, which has a distinctive architecture. The hallmark of IMC is arrangement of eosinophilic tumor cells in a solid, tubular, or morular pattern (3). Mammography depicts irregular or round shaped, high-density mass with spiculated margins, with or without calcification. Homogeneously hypoechoic, microlobulated irregular masses with or without posterior acoustic attenuation are characteristic US findings. MRI findings are not helpful in distinguishing the lesions from invasive ductal carcinomas (18). Fig. 6 shows an IMC in a 54-year-old woman.

Osteoclastic giant cell breast carcinoma

Osteoclastic giant cell breast carcinoma is a very rare type of breast tumor and cannot be radiologically differentiated from other malignant lesions. It is coarsely defined as a breast tumor containing osteoclast-like giant cells. However, these giant cells are specific macrophages, which are distinct from osteoclasts and other giant cells such as foreign body giant cells (3, 19). Histopathologic findings include plenty of multinuclear giant cells, within malignant clusters of epithelial cells among mononuclear stromal cells. Several pathologists reported this carcinoma as a subtype of metaplastic carcinoma (3). However, unlike metaplastic carcinomas, osteoclastic giant cell breast carcinoma does not contain chondro-osseous metaplasia. Diagnosis is solely possible by histologic examination. These lesions can be interpreted as benign entities, such as cyst or fibroadenoma, because of their well outlined nature (19). Fig. 7 shows an osteoclastic giant cell breast carcinoma in a 34-year-old woman.

Malignant phyllodes tumor

Malignant phyllodes tumor, previously known as cystosarcoma phyllodes or periductal stromal tumor, is a lobulated and well-demarcated solid tumor with homogeneous or heterogeneous echo-texture. Approximately 20% of phyllodes tumors are malignant. They rarely metastasize to axillary lymph nodes but hematogenous metastasis to bone and lung is possible. Phyllodes tumor is characterized by proliferation of epithelial and mesenchymal cells (3). It is considered to be a giant form of intracanalicular fibroadenomas, which usually occurs between 10 and 86 years of age. Subjects between 35 and 45 years are considered at high risk for breast cancer (20). They are uncommon under the age of 30, seen in older ages in contrast to fibroadenomas. Accurate differentiation of benign or malignant diagnosis cannot be made only clinically. If the longest dimension of a tumor mimicking fibroadenoma reaches more than 4 cm and grows rapidly, the radiologist should consider the diagnosis of phyllodes tumor. Phyllodes tumors are classified into benign, low-grade malignant (borderline) and high-grade malignant types depending on histologic findings and dimensions (3). Discrimination of fibroadenomas from phyllodes tumors cannot be made by US or mammography. However, phyllodes tumor should be kept in mind, particularly in the presence of clefts or round cysts within solid masses on US (21). Fig. 8 shows a case of malignant phyllodes tumor in a 46-year-old woman.

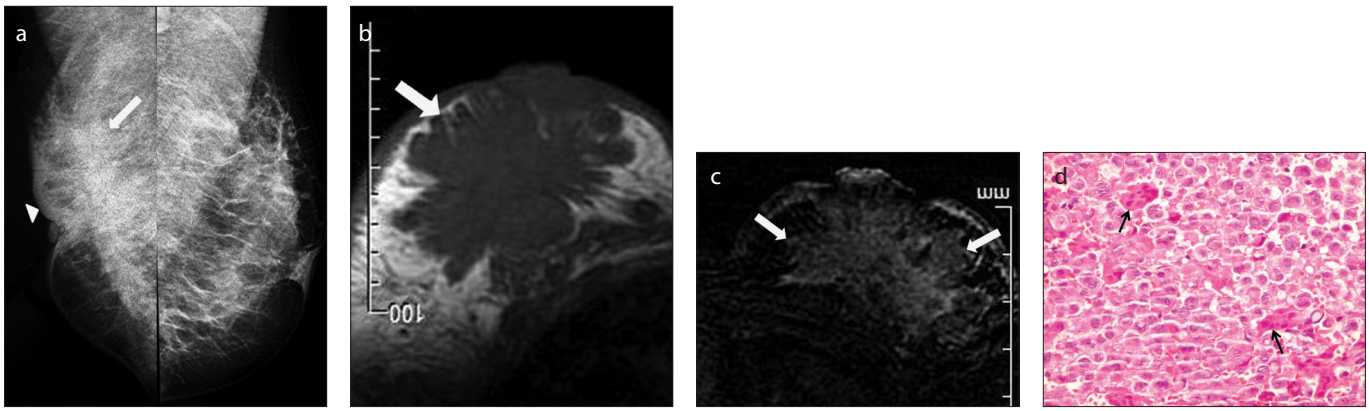

Figure 7. a–d. Osteoclastic giant cell breast carcinoma. Right MLO projection of mammography **(a)** shows an irregular, high-density lesion with indistinct margin *(arrow)*, adjacent skin thickening *(arrowhead)* and axillary lymphadenopathy. Axial T1-weighted image **(b)** shows an irregular mass *(arrow)*. The lesion was categorized as BI-RADS category 5. Subtraction image **(c)** reveals heterogeneous enhancement *(arrows)*. The lesion demonstrated wash-out kinetic (not shown). Histopathologic examination **(d)** (H-E, ×100) demonstrates carcinoma containing osteoclast like multinuclear giant cells *(arrows)*.

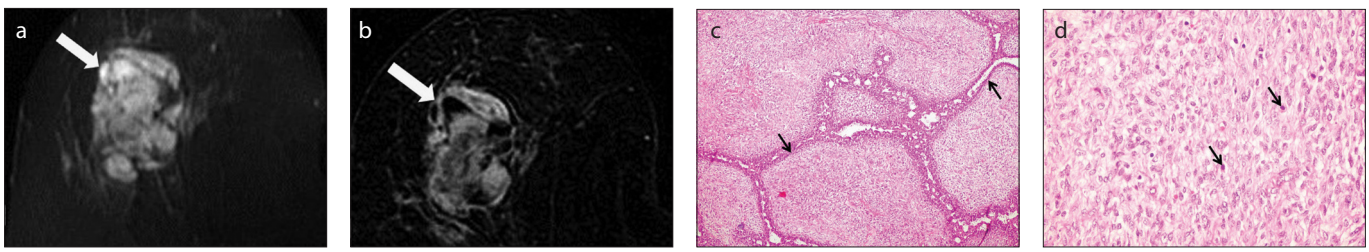

Figure 8. a–d. Malignant phyllodes tumor. Axial T2-weighted image **(a)** shows an irregular and markedly hyperintense lesion *(arrow)* compared with fibroglandular tissue. Subtraction image **(b)** reveals heterogeneous enhancement *(arrow)*. The lesion demonstrated wash-out kinetic (not shown). The lesion was categorized as BI-RADS category 4c. Histopathologic examination (**c,** H-E, ×20) demonstrates leaf-like pattern consisting of slits lined with double stratified epithelium *(arrows)* surrounded by stromal proliferation and (**d,** H-E, ×100) increased number of atypical mitosis *(arrows)* of malignant phylloid tumor.

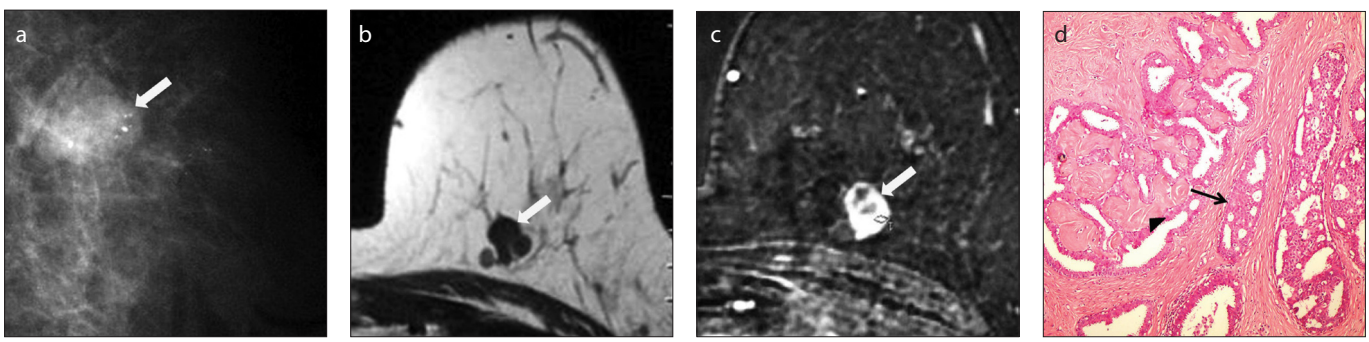

Figure 9. a–d. Carcinoma arising in fibroadenoma. Left MLO projection of mammography **(a)** shows an oval mass with partially obscured margins in which microcalcifications developed during follow-up *(arrow)*. Axial T1-weighted image **(b)** shows a round, circumscribed, hypointense mass *(arrow)* compared with fibroglandular tissue. Subtraction image **(c)** reveals heterogeneous enhancement *(arrow)*. The lesion demonstrated wash-out kinetic (not shown). The lesion was categorized as BI-RADS category 4c. Histopathologic examination **(d)** (H-E, ×20) demonstrates canalicular structures *(arrows)* with low pleomorphism in a hyalinized fibrous stroma *(arrowhead)*, sharply delineated from neighboring tissue inconsistent with fibroadenoma.

Carcinoma arising in fibroadenoma

Breast fibroadenoma is a common benign tumor. Rarely, carcinoma may arise within fibroadenoma. Most of the carcinoma arising in fibroadenoma are in situ carcinomas. Carcinoma rate in fibroadenoma is estimated at about 0.02% (22). It may occur in any age. 44 was reported as mean age in a study (23). The most common carcinoma arising in fibroadenoma is lobular carcinoma in situ (66.9%), followed by ductal carcinoma in situ (12.4%), invasive ductal carcinoma (11%), and invasive lobular carcinoma (3.4%) (3). Sometimes malignant transformation may remain limited within fibroadenoma. Unfortunately, there are no distinctive clinical or imaging findings regarding this entity. If there are any microcalcifications in a fibroadenoma, it may be a clue for intraductal carcinoma. Fig. 9 shows a carcinoma arising in fibroadenoma in a 43-year-old woman.

Metastasis

About 1%–2% of breast malignancies are metastatic lesions. The most common primary site is contralateral breast tumor (3). Other malignancies that metastasize to breast are lymphoma, melanoma, soft tissue sarcomas, granulocytic sarcoma, lung cancer, stomach cancer, prostate cancer, ovarian cancer, and cervix cancer. Metastases are usually seen as solid, multiple masses demonstrating unilateral involvement in 85% of cases (3). Metas-

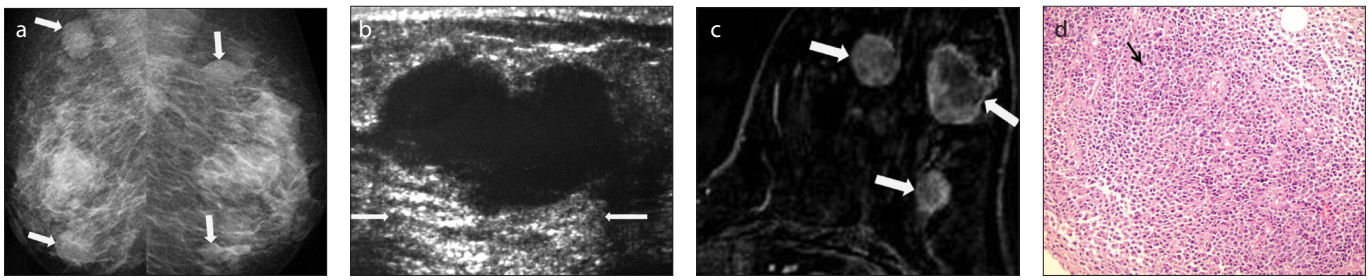

Figure 10. a–d. Metastasis. Bilateral MLO projections of mammography **(a)** show multiple round and oval, high density and noncalcified lesions with obscured margins *(arrows)*. Axial grey-scale US image **(b)** shows markedly hypoechoic and microlobulated, parallel and not parallel lesions with posterior acoustic enhancement *(arrows)*. Subtraction image **(c)** reveals heterogeneous enhancement *(arrows)*. The lesion demonstrated wash-out kinetic (not shown). The lesion was categorized as BI-RADS category 5. Histopathologic examination **(d)** [H-E, ×20] demonstrates prominent monoclonal proliferation of plasma cells *(arrow)* with coarse chromatin material and eosinophilic cytoplasm.

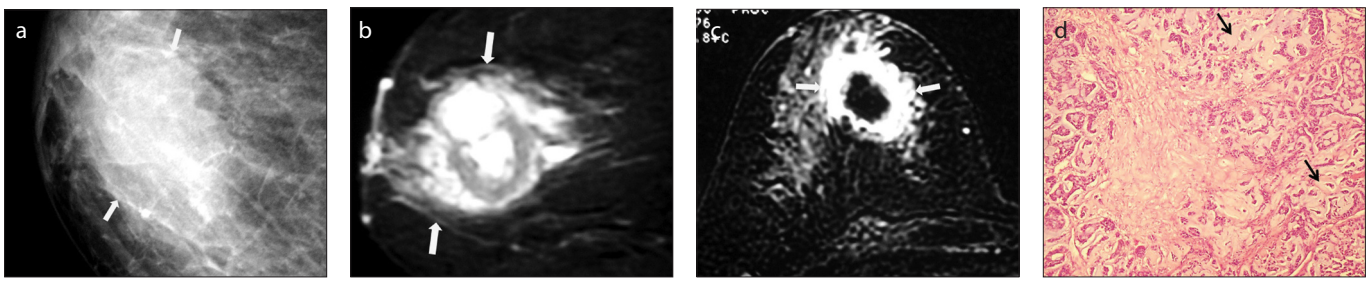

Figure 11. a–d. Metaplastic carcinoma. Right CC projection of mammography **(a)** shows an oval, high density lesion *(arrows)* with obscured margin. Sagittal T2-weighted STIR image **(b)** shows an oval mass *(arrows)* with irregular margin. Subtraction image **(c)** reveals rim enhancement *(arrows)*. The lesion demonstrated wash-out kinetic (not shown). The lesion was categorized as BI-RADS category 5. Histopathologic examination **(d)** (H-E, ×20) demonstrates invasive carcinoma consisting areas of chondroid differentiation *(arrows)*.

tases usually do not cause retraction of the skin or nipple. At mammography, metastatic lesions may manifest as single or multiple masses or as diffuse skin thickening. Involvement might be unilateral or bilateral. They usually appear as round masses with circumscribed or ill-defined borders. Spiculations and microcalcifications might be seen but are rare. Differential diagnosis of breast metastasis should include secondary involvement of breast with multiple myeloma. Fig. 10 shows multiple myeloma metastases to the breast in a 56-year-old woman.

Metaplastic carcinoma

Metaplastic breast carcinoma (MBC) is defined as adenocarcinoma with homogeneous or heterogeneous metaplastic components (3). They are known as ductal carcinomas showing metaplastic amendments by nonglandular growth (24). These tumors are generally rapidly growing palpable masses. Metaplastic carcinomas can present with imaging features similar to malignant and even benign lesions. The age of patients are usually over 50 years. Subjects present with a palpable mass and enlarged axillary lymph node (25). MBCs account for less than 1%–3.7% of all breast carcinomas (3). Metaplastic carcinomas are composed of two distinct metaplasia pattern: squamous and heterologous or pseudo-sarcomatous metaplasia. Hormone receptor gene and oncogene expressions are extremely low in MBC, which may occasionally emerge from underlying fibroadenoma or phyllodes tumor. Imaging features have been variously described such as well-circumscribed, irregular, or spiculated (26); circumscribed, noncalcified, spiculated (24); oval, indistinct, and partially well-circumscribed (27). Metaplastic carcinoma should be kept in mind in the differential diagnosis of noncalcified, predominantly circumscribed masses visualized by mammography. Common radiologic manifestations of metaplastic carcinomas on mammography include high-density and multilobulated or ill-defined masses, occasionally including microcalcifications (%25) (28). They usually do not cause skin retraction or distortion. Particularly tumors with chondroid or osseous metaplasia can demonstrate macrocalcifications mammographically. US reveals cystic and solid components and heterogeneous echo-texture consistent with necrotic component and microlobulated margins. On MRI T1-weighted signal is nonspecific as it is isointense to breast tissue, but T2-weighted signal is mostly high (%91) as a result of necrosis within tumor or chondroid metaplasia unlike most invasive cancers. Therefore, in this respect, metaplastic carcinomas should be differentiated from mucinous carcinoma or infiltrating ductal carcinoma by the presence of necrotic components. In DCE-MRI they usually depict ring-like contrast enhancement pattern, a possible association with central necrosis. Fig. 11 shows a metaplastic carcinoma case in a 36-year-old woman.

Conclusion

Rare lesions of the breast could be easily misdiagnosed as frequent masses because of severe overlap in imaging features between these lesions and the common ones. Histopathologic examination is necessary in the evaluation of such breast lesions, particularly when radiologic images are not definitive for a specific diagnosis.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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