

Imaging the Male Breast

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Abstract

Purpose of Review In this article, we review the clinical and imaging features of a variety of benign and malignant processes of the male breast, with focus on more common entities and those with specific imaging characteristics that may improve diagnostic accuracy.

Recent Findings We emphasize utilization of appropriate imaging modalities according to the age-based protocols provided by the American College of Radiology Appropriateness Criteria in the evaluation of the symptomatic male breast (Mainiero et al., J Am Coll Radiol 12:678–682, 2015).

Summary Based on review of the current literature, we discuss the risk factors, clinical and imaging features, and treatment of male breast cancer, focusing on any gender differences.

Keywords Male breast disease · Breast cancer · Gynecomastia · Male breast imaging

Introduction

Male patients are increasingly referred to breast imaging centers [1]. This is often the case when there is concern that breast cancer is in the differential diagnosis of the patient's presenting signs and symptoms. The etiologies of male

breast pathology are numerous and include both benign and malignant entities [2]. While the most critical reason to image a male patient's breast is to evaluate for malignancy, imaging plays an important role in clinical management of benign male breast conditions as well. The establishment of a benign diagnosis, most commonly due to gynecomastia, can help the clinician seek the stimulating etiology and at the same time reassure the patient that he does not have a breast malignancy.

Male Breast Anatomy

A basic understanding of male breast anatomy is useful for accurate interpretation of clinical and imaging findings. It also helps classify male breast pathology based on cell origin. Before puberty, the male breast is similar to the female breast in that it is composed of lobules that drain through ducts into the nipple. The testosterone surge during puberty causes involution of most of the ducts. The normal adult male breast consists primarily of skin, subcutaneous fat, atrophied blind-ending ducts, and stroma, with lobular development being extremely rare [3•, 4••]. Hence, unlike in females, lobular-derived lesions such as cysts, fibroadenomas, and other lobular neoplasms are exceedingly rare in men.

Clinical Presentation

Breast-related complaints in the male patient most commonly include a palpable lump, tenderness, or enlargement. The importance of a careful breast exam in the evaluation of these symptoms cannot be overemphasized. Clinical exam has been shown to have high sensitivity in the detection of malignancy [5]. However, the differentiation between benign and malignant entities may be difficult

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with physical exam alone. In particular, the distinction between gynecomastia and malignancy may depend on the experience and comfort level of the clinician.

Role of Imaging

Imaging plays an important role in the evaluation of male breast conditions as it improves specificity when combined with physical exam [5]. However, imaging is only indicated when the clinical exam shows indeterminate or suspicious findings [6••]. Given the rarity of male breast cancer, most imaging-based diagnoses are due to non-malignant causes, with up to 97% reported benign in one series [5]. While conventional 2D mammography is the most frequently used imaging modality for the evaluation of male breast disorders, ultrasound can be helpful as both a diagnostic modality as well as to guide tissue sampling. More recently, the use of tomosynthesis to image benign male breast entities has also been reported [7].

Benign Entities

Most benign etiologies of male breast conditions can be categorized into gynecomastia, fat-containing lesions, skin findings, vascular lesions, and cystic masses. Several rarer miscellaneous categories of benign neoplasias such as myofibroblastoma, (Fig. 1) a stromal tumor, are also reported in the literature [2, 8, 9].

Gynecomastia

Gynecomastia refers to a benign proliferation of ductal and stromal elements, with resultant breast symptoms (Fig. 2). It may occur in a unilateral or bilateral fashion and may be symmetric or asymmetric. It is the most common male breast condition [3, 4], occurring in 32–65% of the male population [10]. Although pathology may show mild cellular atypia, this is an expected finding [10] and does not portend a higher risk of breast cancer. The typical age at presentation excluding newborns is bimodal and includes the peri-pubertal age group as well as men over 50 years of age [1]. There are a variety of causes, categorized into idiopathic, physiologic, drug-related, systemic (liver or kidney disease), or hormonal [3, 4, 11]. Treatment is varied and related to etiology, ranging from reassurance, discontinuation of certain drugs/medications to rarely reduction mammoplasty [1, 12].

There are three types of gynecomastia, each of which have typical imaging features and can indicate stage of disease. The nodular form is the early phase of proliferation and indicates less than 1-year duration of symptoms, typically pain. On mammography, it presents as a fan-

shaped subareolar density, blending into surrounding subcutaneous fat. The dendritic form is the later fibrotic phase, causing usually irreversible clinical and imaging findings. It appears as a flame-shaped subareolar density, with characteristic linear projections into adjacent fat. The diffuse glandular form is seen in patients receiving high-dose estrogen. On mammography, findings closely resemble that of the female breast, with bilateral heterogeneously dense breasts.

The most common clinical features include a soft, rubbery or firm, mobile central subareolar mass, with pain in the early phase (particularly <6 months) [6••]. Features that may help distinguish it from a malignant process include pain and central location. However, the nodular/fibrotic form of gynecomastia may present as a painless firm mass, making the distinction from malignancy difficult [5].

Based on both the recent American Academy of Family Physicians (AAFP) guidelines and American College of Radiology (ACR) appropriateness criteria, a male patient of any age with typical symptoms and physical exam findings of gynecomastia should be diagnosed on the basis of clinical findings alone without the need for imaging [6••, 13]. In fact, there are data to suggest that if a recent prior chest CT (performed for other indication) shows findings of gynecomastia in a patient with classic symptoms, a mammogram may not be necessary for further evaluation [14].

However, if the clinical features are indeterminate or suspicious, further evaluation with imaging may be obtained. In patients less than age 25, ultrasound is the initial imaging modality of choice, focused on the site of palpable concern. However, since gynecomastia and other fat-containing entities may appear suspicious on ultrasound, mammography is recommended prior to biopsy recommendation. In patients over age 25, mammography is the initial imaging modality of choice. Given that mammography is highly reliable in the diagnosis of gynecomastia, it may obviate the need for ultrasound and invasive procedures [15]. A bilateral diagnostic mammogram is routinely performed; however, there are no data to suggest superior efficacy over unilateral mammogram [6••]. In addition to gynecomastia, mammography has high sensitivity and specificity in the diagnosis of several fat-containing benign entities.

Fat-containing Entities

Pseudogynecomastia

Pseudogynecomastia refers to increased subareolar fat without proliferation of the glandular component. Clinically, these patients present with breast enlargement rather than a subareolar mass. In cases of indeterminate physical

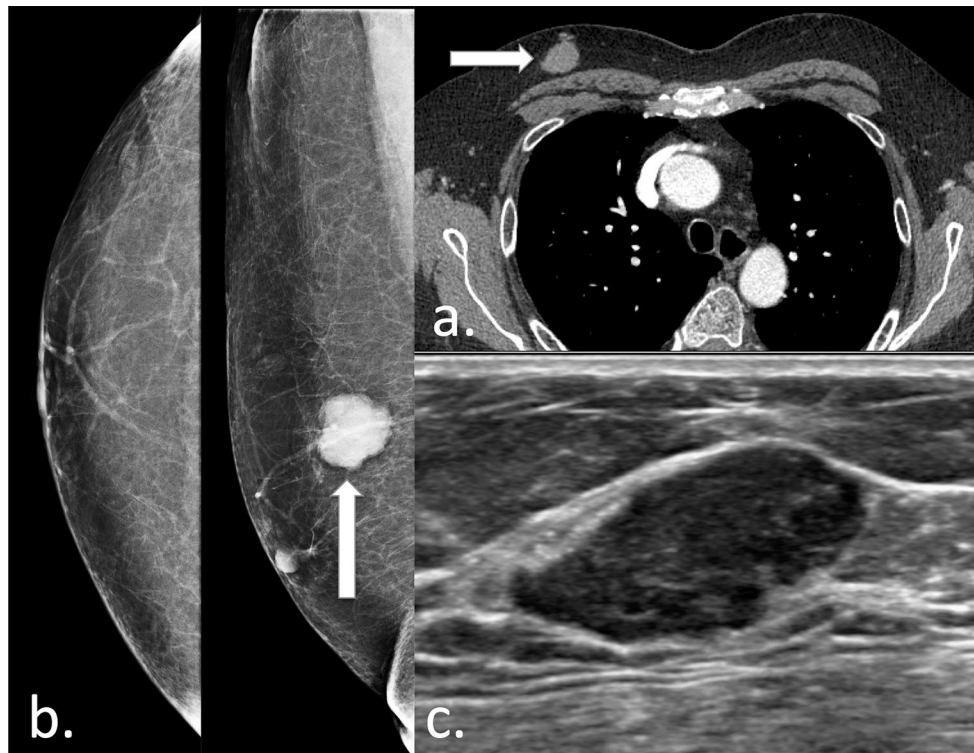


Fig. 1 A 74-year-old man referred to breast imaging for follow-up of incidentally found right breast mass (*arrow*) on chest CT (**a**). Mammogram (**b**) shows a dense, circumscribed mass on the mediolateral oblique (MLO) view (*arrow*) not seen on the

craniocaudal (CC) projection given its medial location. Ultrasound (**c**) shows a circumscribed, oval hypoechoic mass. Histopathology revealed myofibroblastoma on core biopsy

exam, a mammogram may be performed. It shows increased lucent subareolar fat, which is diagnostic [4].

Lipoma

Lipoma is a benign neoplasm composed of mature fat cells with no malignant potential. It is the second most common benign finding of the male breast, after gynecomastia [16]. Clinically, it may present as a soft, mobile, non-tender palpable mass. If identified on mammogram, it appears as an encapsulated oval fat density lesion; however, it may be hard to distinguish from surrounding normal fatty background (Fig. 3). It has a variable appearance on ultrasound—it is usually mildly hyperechoic without significant internal flow. Lipomas may be surgically excised if cosmetically indicated [3, 4].

Angiolipoma

Angiolipoma is an extremely rare benign neoplasm of the breast. As the name suggests, it is composed of mature fat cells and vessels. Unlike lipomas, these tumors can present with pain. On mammogram, it appears as a mixed fat and soft tissue density mass. These benign fat-containing neoplasms may be followed or excised [3].

Lymph Node

Intramammary lymph nodes may be present anywhere in the breast; however, most commonly appear in the upper outer quadrant. It is mammographically identified as an oval or reniform circumscribed mass with a dense outer cortex and lucent fatty central hilum. The sonographic features of a normal lymph node include a homogenous thin (<2 mm) cortex and echogenic fatty hilum [3].

Fat Necrosis and Hematoma

Posttraumatic changes in the breast have specific imaging features that allow for differentiation from other entities and must be considered when there is a history of trauma or coagulopathy. In the acute setting, hematoma and fat necrosis may mimic malignancy on ultrasound, possibly appearing as an irregular mass with indistinct borders difficult to distinguish from a solid mass. However, over time, hematomas and fat necrosis may evolve into more well-defined masses with fluid–debris levels, which may be assessed for mobility on ultrasound by changing position or with real-time imaging using color or power Doppler. There should be absence of internal vascularity. On mammogram, peripherally calcified oil cysts, sometimes

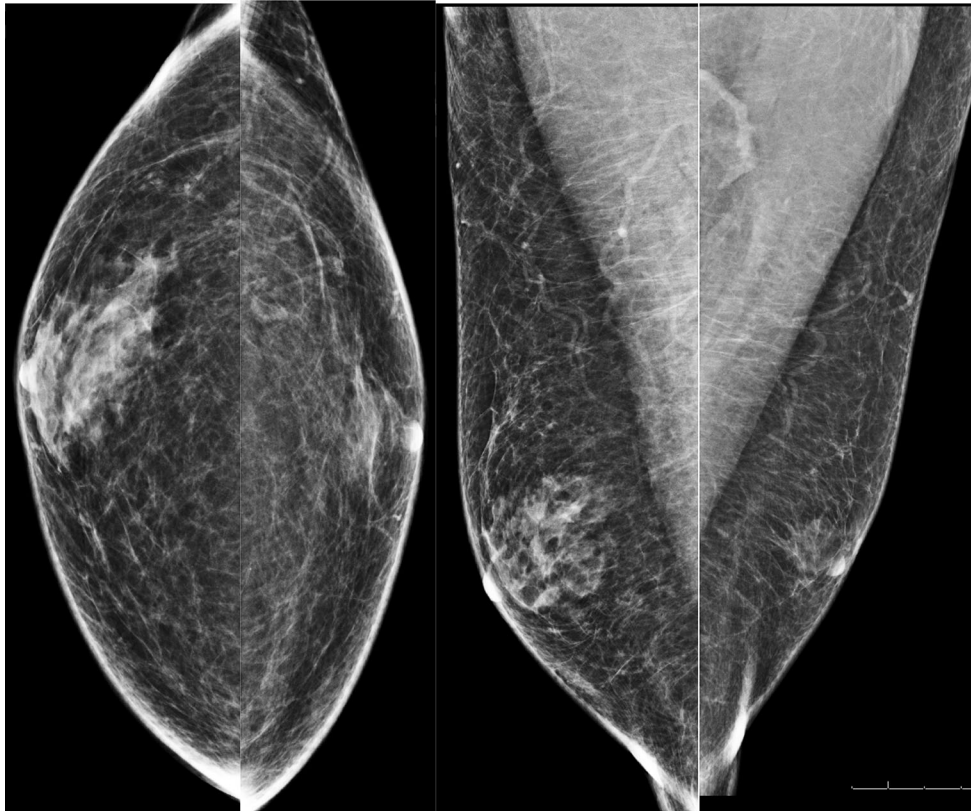


Fig. 2 CC and MLO views of both breasts showing bilateral asymmetric gynecomastia in a 68-year-old man who presented with bilateral breast tenderness

with fat-fluid levels and the eventual formation of dystrophic calcifications are characteristic of fat necrosis [3, 4]. The diagnosis is usually made in the appropriate clinical setting along with typical mammographic (Fig. 4) and ultrasound findings. Short-term follow-up helps ensure expected evolution.

Skin Findings

Sebaceous Cyst/Epidermal Inclusion Cyst

A sebaceous cyst is a benign intradermal lesion that forms due to an obstructed sebaceous gland. An epidermal inclusion cyst is another benign intradermal lesion that forms due to an obstructed hair follicle or secondary to previous skin trauma. These two entities are indistinguishable on imaging. On mammography, they may appear as an oval, circumscribed, dense, superficial mass. Diagnosis may be confirmed on ultrasound, where continuity with the skin is better identified as the claw sign or as a tract leading from the mass to the skin. Biopsy is not recommended as long as imaging features are characteristics due to the risk of inflammatory response caused by cyst rupture [3, 4].

Vascular Lesions

Hemangioma

A hemangioma is a benign neoplasm composed of vascular channels. Figure 5 shows the typical imaging features including an oval-shaped solid mass with circumscribed margins growing parallel to the chest wall. Biopsy is necessary for diagnosis as there are no definite distinguishing features from malignancy. Once the diagnosis is made, surgical excision may be performed to exclude the possibility of angiosarcoma [17].

Venous Malformation

Venous malformations are the most common vascular malformation of the male breast. They are classified as low-flow malformations, made up of endothelial-lined vascular sinusoids. They present in childhood or early adulthood as a long-standing soft, compressible, non-pulsatile painless unilateral breast mass or enlargement. On mammogram, they appear as multiple tubular densities. Typical sonographic features include a multiseptated cystic mass with spectral Doppler showing slow venous flow [3].

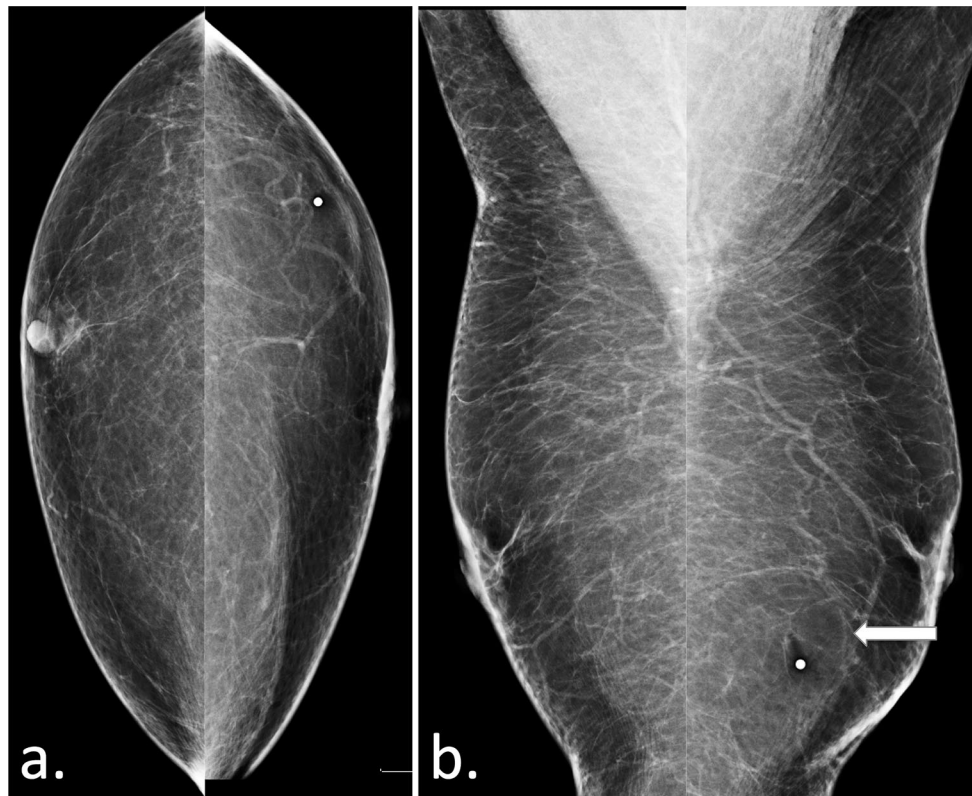


Fig. 3 CC (a) and MLO (b) views show a palpable lump denoted by BB marker. An oval, encapsulated fat density mass is best demonstrated on the MLO view (arrow) consistent with a lipoma

Diagnosis may be made on the basis of clinical and imaging features. Treatment is with percutaneous sclerotherapy.

Other Vascular Lesions

There are numerous other rarer vascular lesions that may occur in the male or female breast including varices, posttraumatic aneurysms, or pseudoaneurysms. Use of color Doppler in the evaluation of cystic lesions is critical for accurate diagnosis and avoidance of aspiration or biopsy.

Cystic Masses

Given the rarity of benign breast cysts in men, any cystic mass in the male breast needs aspiration or biopsy for definitive diagnosis [18]. The exception would be a breast hematoma, as this diagnosis may be made on the basis of history, physical exam with diminution, and evolution expected on follow-up imaging. The differential diagnosis of a cystic mass, which may present with or without nipple discharge, includes a subareolar abscess, papilloma, or malignancy.

Subareolar Abscess

A subareolar abscess is a localized infection from chronic ductal obstruction and inflammation. Clinical features include pain, erythema, nipple swelling, and discharge. On mammography, it appears as an ill-defined subareolar mass with surrounding trabecular thickening; however, it may be difficult to distinguish from gynecomastia or malignancy without the relevant clinical history. On ultrasound, an indistinct complicated fluid collection is seen with mostly peripheral vascularity indicative of hyperemia. However, as these features may mimic malignancy on imaging, aspiration may be necessary for both diagnostic and therapeutic reasons [3, 16] (Fig. 6).

Papilloma

Papilloma is a neoplasm resulting from benign epithelial proliferation, supported by a fibrovascular core. Clinically, it may present as a palpable mass or nipple discharge. Mammography may show a dense, circumscribed, retroareolar mass. Ultrasound is more sensitive and typically shows an intraluminal mass within a dilated duct. Due to the relatively high proportion of male papillary

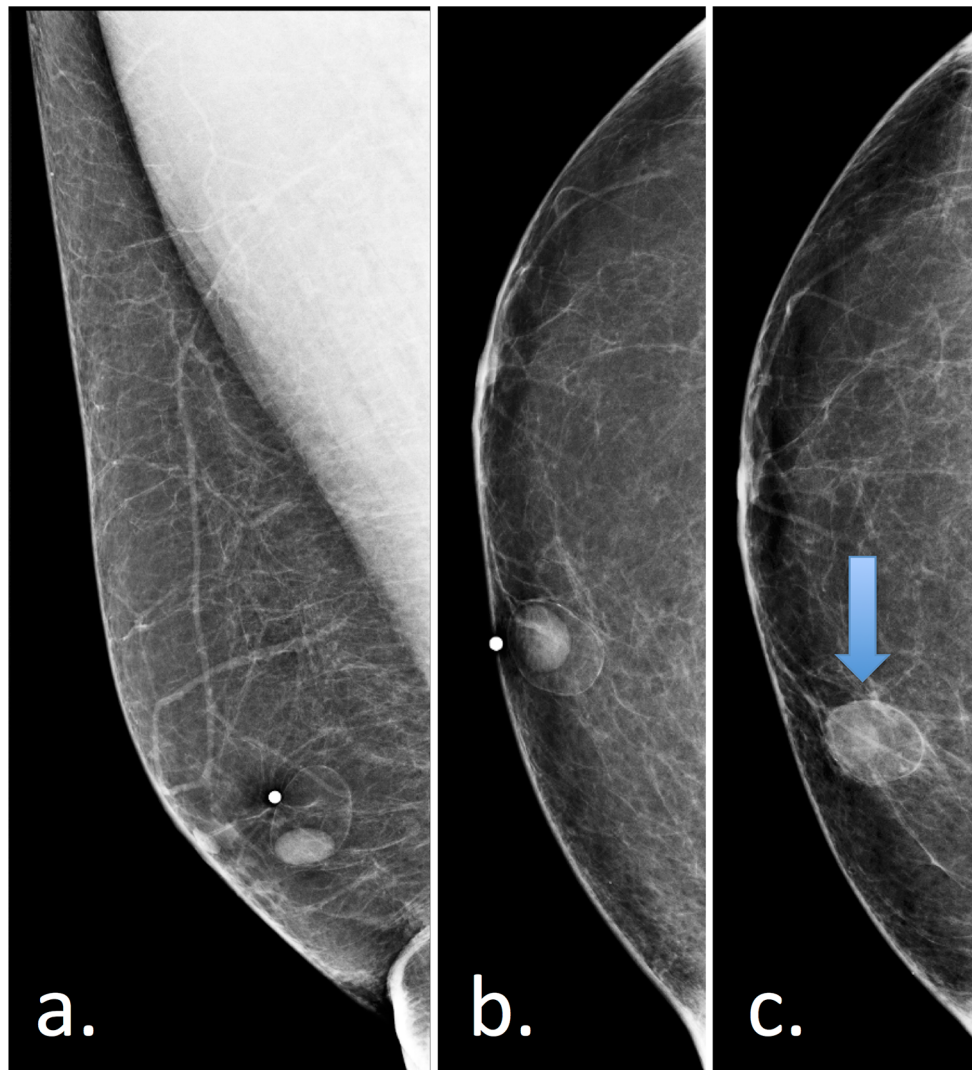


Fig. 4 MLO (a) and CC (b) views of the right breast with BB marker indicating a palpable lump 2 months after being hit in the chest while playing racquetball. Repeat CC (c) view 6 months after initial presentation shows evolving fatty mass due to fat necrosis

carcinoma [19] and the potential of sampling error associated with core-needle biopsy, surgical excision is frequently recommended for all papillary lesions in the male breast [16].

Malignant Entities

Breast Cancer

Incidence and Risk Factors

The incidence of male breast cancer in the United States in 2016 was 2600, with 440 estimated deaths [20]. Less than 1% of breast cancers occur in men [3]. There are several risk factors for male breast cancer, most of which are similar to those for female breast cancer including

family history, previous chest irradiation, and increased estrogen states. Recently, obesity has been stressed as a significant risk factor [21•]. A significant association between a history of testicular conditions such as orchitis/epididymitis and male breast cancer has also been found [21•, 22].

Gynecomastia has been suggested as a risk factor for breast cancer [21•]; however, the causal relationship is difficult to establish as both entities have common hormonal risk factors. For example, hormonally related conditions such as Klinefelter syndrome have a strong association with both gynecomastia and male breast cancer. However, gynecomastia is highly prevalent among males, whereas breast cancer represents only a very small percentage (1–2% [23, 24]) of symptomatic male breasts. Hence, gynecomastia by itself is not believed to be a significant risk factor for breast cancer.

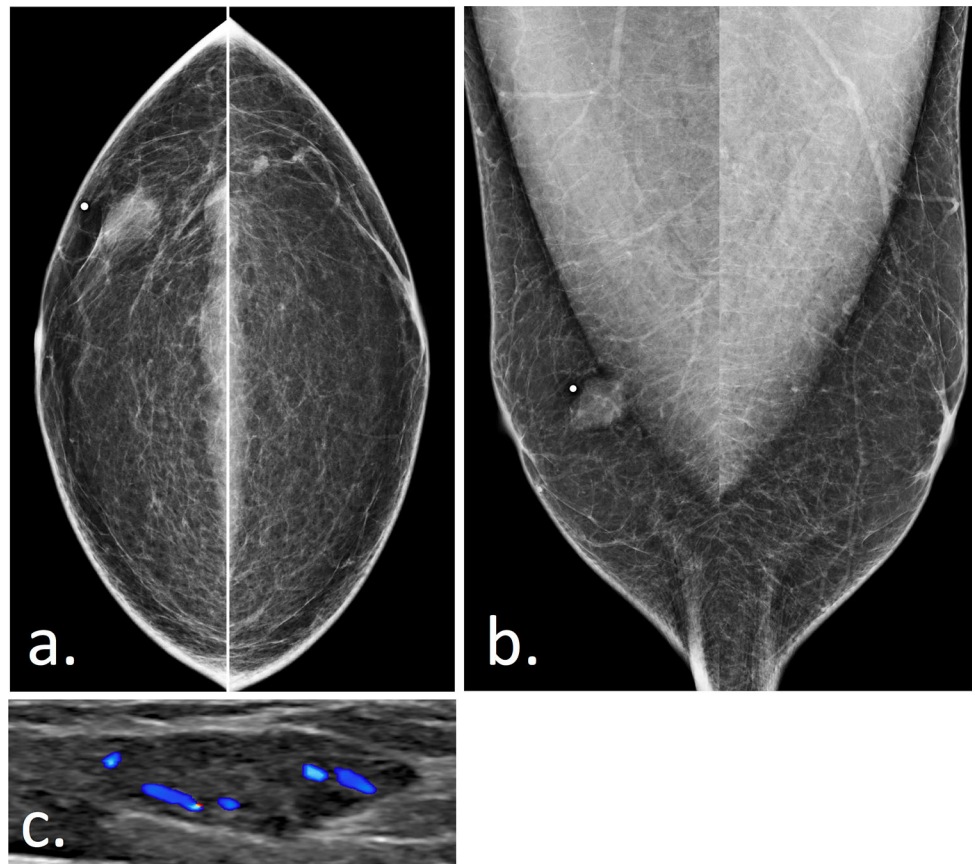


Fig. 5 A 45-year-old man was referred for breast imaging of a palpable lump in the right breast. CC (a) and MLO (b) views show a circumscribed, oval mass corresponding to the patient's palpable

finding indicated by a BB marker. Ultrasound (c) demonstrates a hypoechoic, oval, vascular mass growing parallel to the skin. The mass proved to be a hemangioma on core biopsy

The BRCA2 mutation is more frequently associated with male breast cancer than BRCA1. The BRCA2-associated male breast cancers tend to present at higher stage and grade than in female BRCA2 carriers, suggesting a different phenotype and biological behavior of the mutation in men [25]. The value of routine screening with mammography in male BRCA2 patients has not been studied and is unknown.

The trend of more advanced stage at presentation in men compared to women may relate to the general lack of awareness, given the rarity of male breast cancer. The 5-year overall survival rate is 74% in men compared to 83% in women; however, disease-specific survival data are limited [26] and male breast cancer patients tend to be older than female patients. In one large series, the mean age at diagnosis in men was 63, which is 4 years older than that of women [26]. In fact, cancer is extremely rare in men less than 45 years of age [5].

The most common malignancy of both the male and female breast is invasive ductal carcinoma, which represents up to 82% of male breast cancers [5, 19]. Hormone receptor-positive disease is more common in men than in

women, reported in up to 88.3% of male breast cancers [25–28]. In one study, Non-Hispanic, African American men were more likely to have triple-negative disease than white men [19, 28], a trend similar to that seen in women. Plasilova and colleagues found that patients with triple-negative and Her 2 + disease present with larger and higher grade tumors, lymphovascular invasion, and metastatic disease than those with hormone-positive, Her 2-disease [19]. Others have also found that men with breast cancer have a higher prevalence of metastatic disease than women with breast cancer [29]. DCIS accounts for 5% of all cases of male breast cancer [3]. Papillary carcinoma represents 2.6% of cases and is more common in men than in women [30, 31].

Clinical Presentation

The most common presentation of male breast cancer is a painless palpable lump. Other secondary signs of malignancy include nipple ulceration, retraction, or discharge, or skin thickening [3]. Although rare, nipple discharge (particularly bloody discharge) is highly suspicious and

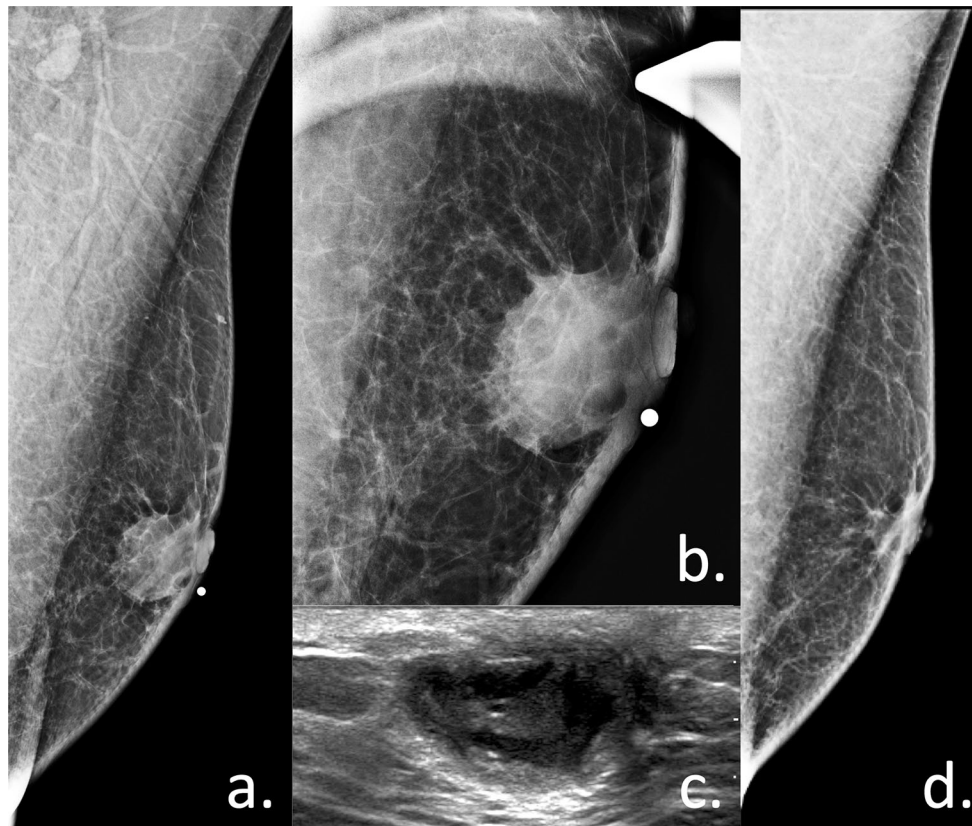


Fig. 6 A 41-year-old man presents with one-week history of a tender palpable lump in the left breast. MLO (a) and magnification view (b) show a subareolar irregular mass with spiculations and subtle skin thickening. Ultrasound (c) demonstrates a subcutaneous mass with heterogeneous echogenicity and possible extension into the dermis.

During ultrasound-guided core biopsy, purulent drainage was noted which was submitted for culture yielding coagulase-negative staphylococcus. No malignancy was found on tissue biopsy. Follow-up mammogram (d) showed resolution of the abscess after completion of antibiotic therapy

considered an early sign of malignancy even in the absence of a palpable mass [5]. Cytology is highly specific but not sensitive for detection of malignancy [5, 32]. A patient with clear or bloody nipple discharge and negative mammogram and ultrasound work up may proceed to breast MR or surgical excision to exclude malignancy.

Physical exam alone has been shown to have lower diagnostic performance than imaging in the diagnosis of male breast cancer, with reported sensitivity in one series as low as 64%. The position of the mass relative to the nipple was not found to be a reliable indicator of malignancy in that study [23]. Yet another study reports high sensitivity but low specificity of physical exam in the evaluation of the symptomatic male breast [5]. In cases of indeterminate or suspicious clinical findings, imaging can aid in diagnosis.

Imaging

The initial imaging modality of choice in the evaluation of clinical findings suspicious for breast cancer is a diagnostic

mammogram. Ultrasound is usually only performed as the next step if mammogram findings are suspicious or indeterminate. Ultrasound helps assess the extent of disease and offers guidance for biopsy. Mammography and ultrasound together have a negative predictive value of close to a 100% [5].

On mammography, breast cancer usually appears as a dense, irregular spiculated mass, eccentric to the nipple (Figs. 7, 8). Mammography is useful for the detection of micro-calcifications—an uncommon but suspicious finding typically seen in DCIS [4, 5]. On ultrasound, findings are similar to female breast cancer, with the most common appearance being an irregular hypoechoic solid mass [16]. Given that up to 47% of men have axillary nodal involvement at time of diagnosis [6••], axillary ultrasound is recommended in men with imaging findings suspicious for breast cancer. The data on the value of MR in the evaluation of male breast disease are limited. A small study shows that benign and malignant entities in male patients have similar features and diagnostic criteria on MR as in female patients [33].

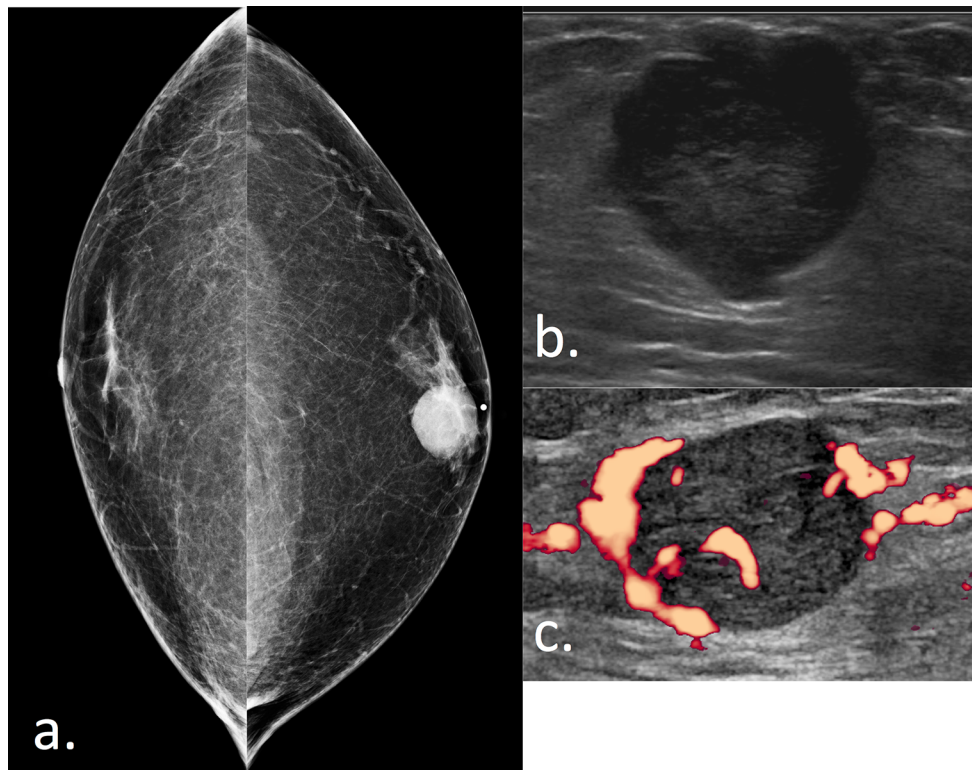


Fig. 7 CC views (a) show a dense, round retroareolar mass corresponding to a non-tender, firm, palpable lump of 6 months duration in an 83-year-old man. On ultrasound (b), the mass is hypochoic and growing anti-parallel to the skin. An enlarged axillary

lymph node with loss of fatty hilum (c) is also shown. Histopathology confirmed intermediate-grade solid papillary carcinoma, ER+, PR+, Her2-, with metastatic axillary node involvement

Treatment

Treatment options for male breast cancer are generally extrapolated from those available for female breast cancer [25, 34]. A large study showed that men are twice as likely as women to undergo mastectomy and less likely to undergo radiotherapy [26]. The study showed similar rates for use of chemotherapy, which suggested underutilization, given more advanced stage at presentation in men. Hormone therapy was received or recommended in only 41.2% of cases; however, this was at least partially attributed to underreporting in the National Cancer Database [26]. Increasing awareness of male breast cancer and following treatment guidelines in place for treating female breast cancer may help improve outcomes in male breast cancer patients.

Other Malignancies

Other malignancies of the male breast include lymphoma and metastases. Most cases of lymphoma are secondary

and of the non-Hodgkin B cell variety. Typical imaging appearance is that of single or multiple circumscribed masses with or without bilateral axillary lymphadenopathy [4, 8]. Metastasis to the breast from extra-mammary source is extremely rare [3].

Conclusion

Evaluation of the symptomatic male breast starts with the clinical history and physical exam. Most findings are benign, with gynecomastia being the most common entity. Imaging may be used only if clinical evaluation is indeterminate or suspicious. Certain key imaging features may aid in the accurate diagnosis of common benign entities. Mammography may clearly show signs specific for gynecomastia or confirm the presence of encapsulated fat within a lesion. Ultrasound may help identify a finding as intradermal, vascular, or confirm posttraumatic changes. All other findings in the male breast, whether solid or

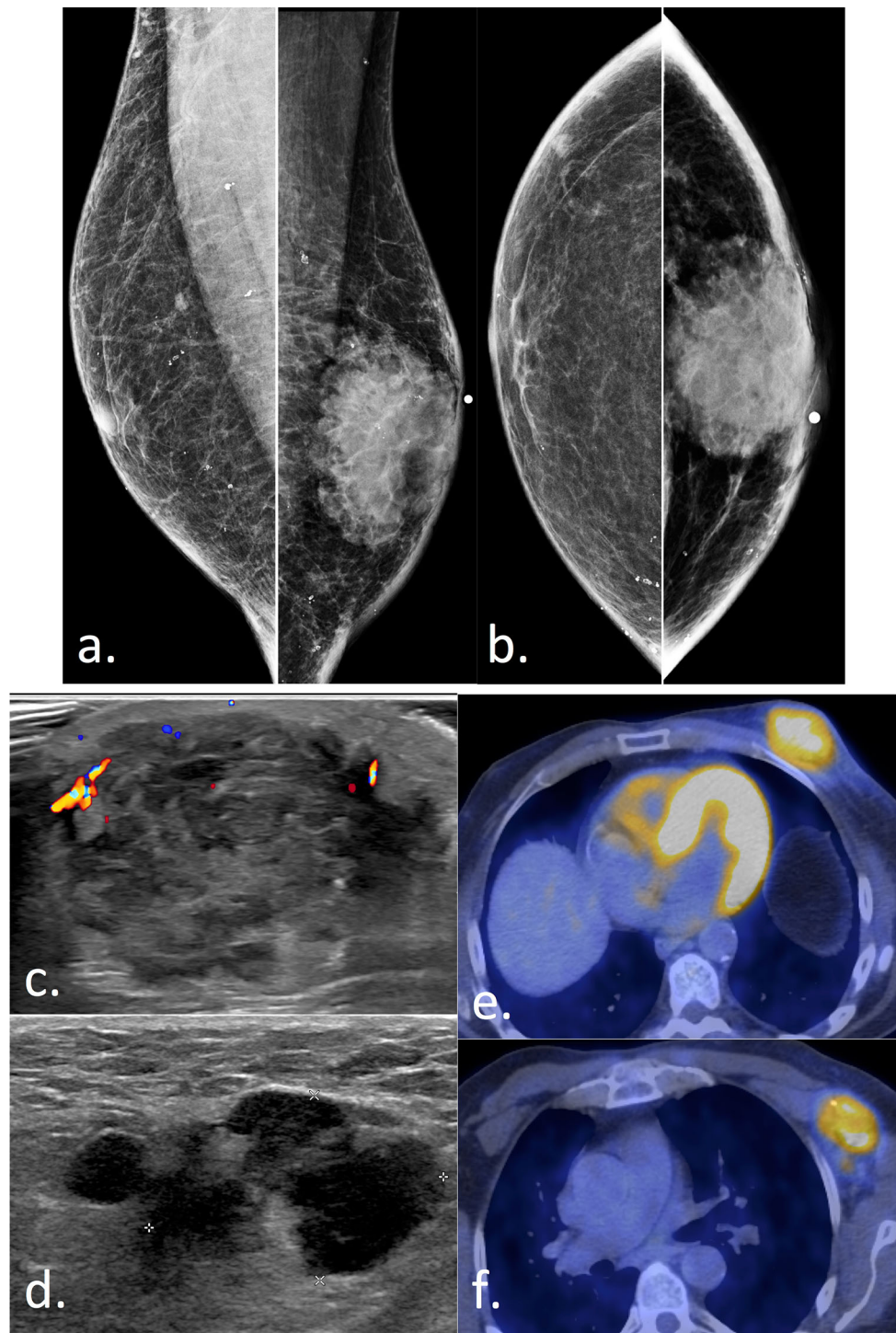


Fig. 8 A 57-year-old man presented with an ulcerating lump. MLO (a) and CC (b) views show a large, irregular, subareolar dense mass with skin thickening. Ultrasound (c) demonstrates a large mass with heterogeneous echogenicity. Evaluation of the axilla shows a pathologically enlarged, possibly necrotic lymph node (d).

Histopathology confirmed metastatic high-grade invasive ductal carcinoma. Staging positron emission tomography images show hypermetabolic masses in the breast (e) and axilla (f) corresponding to known metastatic malignancy

cystic, need tissue sampling for definitive diagnosis. Although male breast cancer is rare, it must be ruled out with biopsy in all cases where imaging is unable to provide a clear benign diagnosis.

Compliance with Ethical Standards

Conflict of Interest Shruthi Ram and Shadi Aminololama-Shakeri each declare no potential conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- Of major importance

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