Granulomatous Mastitis in a Transgender Patient

Kenny Q Sam[1*], Frederick J Severs[1], Lilian O Ebuoma[1], Nagi S Chandandeep[2], Emily L Sedgwick[1]

1. Department of Diagnostic and Interventional Radiology, Baylor College of Medicine, Houston, USA

2. Department of Pathology and Immunology, Baylor College of Medicine, Houston, USA

* **Correspondence:** Kenny Sam, D.O., One Baylor Plaza, Houston, TX 77030, USA
(*Kenny.sam2@bcm.edu*)

Radiology Case. 2017 Feb; 11(2):16-22 :: DOI: 10.3941/jrcr.v11i2.2934

ABSTRACT

Granulomatous mastitis is a rare and benign inflammatory condition of the breast most commonly affecting women of child-bearing age as well as patients on oral contraceptives. This condition is important to identify due to its diagnostic mimicry of malicious entities such as breast carcinoma. Clinical and radiological findings are nonspecific and may overlap with breast carcinomas, thus pathologic confirmation is often necessary for definitive diagnosis. Although cases of granulomatous mastitis have been described in cisgender females, there have been no reported cases in the transgender patient, a growing patient population with few imaging guidelines. Transgender patients are at risk of developing this breast entity due to the use of long-term hormone treatments or presence of residual breast tissue. A trial of antibiotics or steroids may be administered. However, surgical treatment is often necessary in recurrent or refractory cases.

CASE REPORT

CASE REPORT

A 36 year old male-to-female (MtF) transgender patient with a history of long term hormonal treatment presented with bilateral palpable breast masses for two months. The patient had been receiving estrogen therapy for six of the past seven years in addition to an anti-androgen, spironolactone, for the past two years. There was no personal or family history of breast carcinoma, and the patient had no prior breast imaging.

A diagnostic mammogram was performed which showed a 5 mm equal density oval mass with circumscribed margins in the right breast at 11 o'clock anterior depth [Figure 1] which correlated with a palpable mass on pre-imaging clinical exam. There was no mammographic or sonographic correlate to the left breast palpable concern. Sonographic evaluation of the palpable abnormality in the right breast demonstrated a non-parallel irregular hypoechoic mass with posterior acoustic shadowing measuring 0.5 x 0.3 x 0.4 cm [Figure 2].

Histopathological examination of this mass revealed acute and chronic inflammation and histiocytic inflammation arranged in poorly formed granulomata [Figure 3]. The mass stained negative for occult epithelial cells (pankeratin immunohistochemical stain), acid-fast bacilli (AFB stain) and fungal organisms (Grocott-Gomori methenamine silver (GMS) stain). No malignancy was seen.

These findings established the diagnosis of granulomatous mastitis. The patient was seen by the breast surgeon, deferred any further treatment, and was subsequent lost to follow up.

DISCUSSION

Etiology & Demographics:

Granulomatous mastitis (GM) most commonly presents in women of child-bearing age, with a mean age of presentation of 33-38 years old, and represents 1.8% of benign breast diseases [1-8]. Although the exact etiology is uncertain, an autoimmune etiology is favored with additional associations to

pregnancy and lactation [3-4, 8]. The hypothesis proposes prolonged breast-feeding results in long term distention of acini and ducts, which increases the risk of injury and rupture of these structures and causes a granulomatous response [8]. GM has also been associated with patients taking oral contraceptives [8-9], although the association with long term hormonal therapy for gender reassignment, such as in our patient, has not yet been elucidated.

Clinical & Imaging Findings:

Granulomatous mastitis has similar physical exam findings as breast carcinoma, making the clinical distinction difficult. GM most commonly present as a palpable breast mass (78-89% of cases), and less commonly with pain or tenderness (11-41%), erythema, skin thickening, sinus formation or axillary adenopathy [2, 4, 8, 10]. Symptoms frequently persist despite various treatment regimens, and may necessitate further diagnostic testing [5, 7]. GM usually occurs unilaterally without side or site predilection, although tends to spare subareolar region [4, 7-8, 11].

Many cases of granulomatous mastitis will need histopathologic confirmation following diagnostic imaging to distinguish this entity from malignancy. Core biopsy is diagnostic in 96% of women, whereas fine needle aspiration is only diagnostic in 21% [5]. Histologically, GM demonstrates nonnecrotizing noncaseating granulomas mixed with epithelioid histiocytes, multinucleated giant cells of the foreign body and of the Langerhans types confined to breast lobules [4-6, 8]. Inflammation often extends into adjacent perilobular and interlobular tissue with frequent microabscess formation and fat necrosis [5, 11]. The predominance of neutrophilic infiltrate in the background and absence of necrosis favor a diagnosis of granulomatous mastitis [4]. Cytologic examination may be unable to differentiate GM from carcinoma or other granulomatous diseases of the breast, subsequently requiring a wide breast tissue sample for differentiation [8].

Imaging characteristics of granulomatous mastitis are often nonspecific. Mammographic evaluation demonstrates variable breast density, with a 56% incidence of heterogeneously dense or extremely dense parenchymal pattern [3, 5, 7-8]. An asymmetry (44%) or irregular mass(es) (16-34%) may also be present, as well as skin thickening (7%) or axillary adenopathy (18%) [2, 5]. Calcifications are rare [7].

Sonographically, GM commonly appears as an irregular hypoechoic mass with a reported mean diameter ranging from 0.8 to 6 cm [5]. These masses may present with or, less commonly, without hypoechoic tubular extensions leading away from the mass [2-3, 5, 11], and often with posterior acoustic enhancement [8]. Perilesional echogenicity may be present, which corresponds to fibrous walls of confluent granulomas [6]. Doppler ultrasound shows increased vascularity of the lesions and surrounding tissues [7]. Yildiz et al. reported fistulae in up to 50% of patients [3].

Magnetic resonance (MR) imaging will demonstrate heterogeneous segmental T1 hypointense and T2 hyperintense signal [12]. These areas correspond to heterogeneous nonmasslike enhancement on postcontrast dynamic T1-weighted sequences with heterogeneously enhancing irregular lesions. The enhancing lesions most often demonstrate gradual enhancement and either progressive (Type 1) kinetics (50%) or plateau (Type 2) kinetics (50%) [8, 12]. Additional MR findings may also include overlying skin thickening or nipple retraction [12].

Treatment & Prognosis:

The optimal management for GM has not been established. Some studies report 50-75% complete remission in patients who did not receive any treatment [11, 13]. Often the clinical presentation is similar to that of a breast infection and abscess, and thus many suspected cases are empirically treated with antibiotics. Surgery can be therapeutic as well as diagnostic. Surgical options include local excision and abscess drainage or wide surgical excision, often dictated by the disease extent [8]. Wide surgical excision is more efficacious than local excision or incision and drainage (I&D) [5, 10], and often times, I&D may ultimately lead to a second operation after confirmation of GM is made. The efficacy of I&D is improved with post surgical steroids [5]. Complications of excisional surgery include chronic sinus formation, poor wound healing, and cosmetic disfigurement [11]. Recurrence rates for surgical excision range from 8-50% [13-14].

Nonsurgical treatments include antibiotic therapy or corticosteroids [2, 5-6, 8]. Due to the similar clinical presentation to breast infection and abscess, antibiotics are typically given as an empiric treatment, despite a 5% efficacy rate [5]. DeHertogh et al. was the first to recommend steroid therapy for the treatment of granulomatous mastitis [15]. Steroid treatments have been shown to be effective either without or with surgical excision, especially in recurrent or resistant cases [2, 8], although there is currently no consensus on the duration and dose of the corticosteroid administration. Infectious etiologies must be excluded before initiating steroids, however, due to possible exacerbative effects of steroids on infection [2, 4]. Refractory or steroid resistant cases may respond to methotrexate, hydroxychloroquine, azathioprine, and/or colchicines [2, 4, 9, 14, 16].

There are relatively few standard recommendations for breast and chest examinations in the transgender population. Mastectomy and chest contouring as part of sex reassignment may leave residual breast tissue, particularly in the axillary region [17], resulting in the possibility of developing breast pathologies in these areas. Additionally, transgender patients will receive cross-sex hormone treatments such as testosterone in the female-to-male population or estrogen and anti-androgens in the male-to-female population, which can theoretically increase the risk of inducing hormone-sensitive cancers such as breast cancer [17-19]. In the transgender patient with prior or current history of hormone use, current guidelines advocate annual mammography beginning at 50 years old if there are additional risk factors which include

estrogen or progestin use for >5 years, body mass index >35, and a family history of breast cancer. Clinical breast examinations are not recommended for formal cancer screening. Routine screening mammography is not recommended in transgender patients with no hormone use unless there are other risk factors, such as Klinefelter syndrome [20]. Although there are studies in the literature documenting the incidence and risks of breast cancer in the transgender population, to our knowledge, our case was the first of granulomatous mastitis in this population to be evaluated and published. Additional research on the non-malignant entities of the transgender breast should be performed to improve standard of care for this growing population.

Differential Diagnoses:

Acute infectious mastitis or breast abscess

Infectious mastitis generally occurs in younger women, often arises from secondary Staphylococcus aureus infection from skin contamination, and may develop an abscess. Risk factors include primiparity, breast feeding, obesity, smoking, and diabetes. Symptoms include skin redness, pain, and heat, and may be associated with a palpable mass. Mammography can demonstrate an asymmetry, mass or architectural distortion with overlying skin thickening, however calcifications are rare. Ultrasound evaluation of infectious mastitis shows nonspecific areas of increased echogenicity correlating with inflamed glandular and fat tissue, occasionally with prominent inflamed axillary lymph nodes. Breast abscesses may appear as multiloculated, hypoechoic collections with peripheral increased echogenicity. Treatment is often percutaneous drainage with concurrent antibiotics. Patients with granulomatous mastitis are often initially unsuccessfully treated for acute infectious mastitis [21].

Inflammatory breast cancer

Inflammatory breast cancer (IBC) is a rare subtype of breast cancer with characteristic dermal-lymphatic invasion. Common clinical symptoms include a rapid onset of breast erythema and edema as well as the characteristic peau d'orange dimpling of the skin. Distinguishingly, IBC will rarely present with a palpable breast mass, which is the most common clinical presentation of granulomatous mastitis. Imaging findings include skin thickening, trabecular thickening, and enlarged lymph nodes with marked cortical thickening. However IBC will less commonly present as multiple masses, calcifications or architectural distortion. MR imaging will demonstrate streaky parenchymal and pectoral fluid signal and enhancing irregular masses, non-masslike enhancement, or reticular pattern corresponding to lymphatic invasion. The standard of care for patients with IBC is pre-operative chemotherapy with surgery for patients with stage III or IV IBC [22].

Invasive breast carcinoma

Breast cancer is the second leading cause of cancer death in women in the United States and will develop in 1 in 1000 men. Most often arising from the terminal duct lobules, the most common subtype of invasive breast cancer has a ductal component. Clinically, symptomatic patients with invasive breast cancer will most often present with a palpable mass or nipple or skin changes. Mammography may show an irregular mass with spiculated or indistinct margins, and its sonographic correlate commonly appears as an irregular, hypoechoic vascular mass often with an echogenic rim. On MR imaging, invasive breast carcinomas often present as an irregular enhancing mass or segmental area of non-masslike enhancement, which demonstrates washout kinetics (Type 3). Treatment regimen includes surgery (breast conservation with adjuvant radiation therapy versus mastectomy) and adjuvant or neoadjuvant chemotherapy. Targeted receptor therapies are also utilized as treatment.

TEACHING POINT

Granulomatous mastitis is a rare and benign entity that is important to consider in the transgender patient due to the history of hormone use and the diagnostic mimicry of breast carcinoma. Imaging findings are nonspecific however, most often present as asymmetries or masses on mammography with associated radiating hypoechoic tubular extensions on sonogram.

REFERENCES

1. Kessler E, Wolloch Y. Granulomatous mastitis: a lesion clinically simulating carcinoma. Am J Clin Pathol 1972;58:642. PMID: 4674439

2. Mohammed S, Statz A, Lacross JS, et al. Granulomatous mastitis: a 10 year experience from a large inner city county hospital. J Surg Res 2013;184:299-303. PMID: 23890401

3. Yildiz S, Aralasmak A, Kadioglu H, et al. Radiologic findings of idiopathic granulomatous mastitis. Med Ultrason 2015;17:39-44. PMID: 25745656

4. Erozgen F, Ersoy YE, Akaydin M, et al. Corticosteroid treatment and timing of surgery in idiopathic granulomatous mastitis confusing with breast carcinoma. Breast Cancer Res Treat 2010;123:447-452. PMID: 20625813

5. Larsen L, Peyvandi B, Klipfel N, et al. Granulomatous lobular mastitis: Imaging, diagnosis, and treatment. AJR 2009;574-581. PMID: 19620458

6. Han BK, Choe YH, Park JM, et al. Granulomatous mastitis: Mammographic and sonographic appearances. AJR 1999;173:317-320. PMID: 10430126

7. Al-Khawari HA, Al-Manfouhi HA, Madda JP, et al. Radiologic features of granulomatous mastitis. Breast J 2011;645-650. PMID: 21929558

8. Ocal K, Dag A, Turkmenoglu O, et al. Granulomatous mastitis: clinical, pathological features, and management. Breast J 2010;16:176-182. PMID: 20030652

9. Sheybani F, Sarvghad MR, Naderi HR, et al. Treatment for and clinical characteristics of granulomatous mastitis. Obstet Gynecol 2015;125(4):801-807. PMID: 25751209

10. Kiyak G, Dumlu EG, Kilinc I, et al. Management of idiopathic granulomatous mastitis: dilemmas in diagnosis and treatment. BMC Surgery 2014;14:66. PMID: 25189179

11. Mahlab-Guri K, Asher I, Allweis T, et al. Granulomatous lobular mastitis. IMAJ 2015;17:476-480. PMID: 26394488

12. Kocaoglu M, Somuncu I, Ors F, et al. Imaging findings in idiopathic granulomatous mastitis: A review with emphasis on magnetic resonance imaging. J Comput Assist Tomogr 2004;28(5):635-641. PMID: 15480037

13. Lai ECH, Chan WC, Ma TKF, et al. The role of conservative treatment in idiopathic granulomatous mastitis. Breast J 2005;11(6):454-456. PMID: 16297091

14. Yabanoglu H, Colakoglu T, Belli S, et al. A comparative study of conservative versus surgical treatment protocols for 77 patients with idiopathic granulomatous mastitis. Breast J 2015;21(4):363-369. PMID: 25858348

15. DeHertogh DA, Rossof AH, Harris AA, et al. Prednisone management of granulomatous mastitis. N Engl J Med 1980;303(14):799-800. PMID: 7191051

16. Akbulut S, Arikanoglu Z, Senol A, et al. Is methotrexate an acceptable treatment in the management of idiopathic granulomatous mastitis? Arch Gynecol Obstet 2011;284:1189-1195. PMID: 21207047

17. Brown GR, Jones KT. Incidence of breast cancer in a cohort of 5,135 transgender veterans. Breast Cancer Res Treat 2015;149:191-198. PMID: 25428790

18. Gooren LJ, van Trotsenburg MAA, Giltay EJ, et al. Breast cancer development in transsexual subjects receiving cross-sex hormone treatment. J Sex Med 2013;10:3129-3134. PMID: 24010586

19. Lawrence AA. 2007. Transgender health concerns. In: Meyer IH, Northridge ME, editors. The health of sexual minorities: public health perspectives on lesbian, gay, bisexual and transgender populations. New York (NY): Springer. 473-505. ISBN: 978-0-387-31334-4

20. Phillips J, Fein-Zachary VJ, Mehta TS, et al. Breast imaging in the transgender patient. AJR 2014;202:1149-1156. PMID: 24758673

21. Trop I, Dugas A, David J, et al. Breast abscesses: Evidence-based algorithms for diagnosis, management, and follow up. Radiographics 2011;31:1683-1699. PMID: 21997989

22. Yeh ED, Jacene HA, Bellon JR, et al. What radiologists need to know about diagnosis and treatment of inflammatory breast cancer: A multidisciplinary approach. Radiographics 2013;33:2003-2007. PMID: 24224593

FIGURES

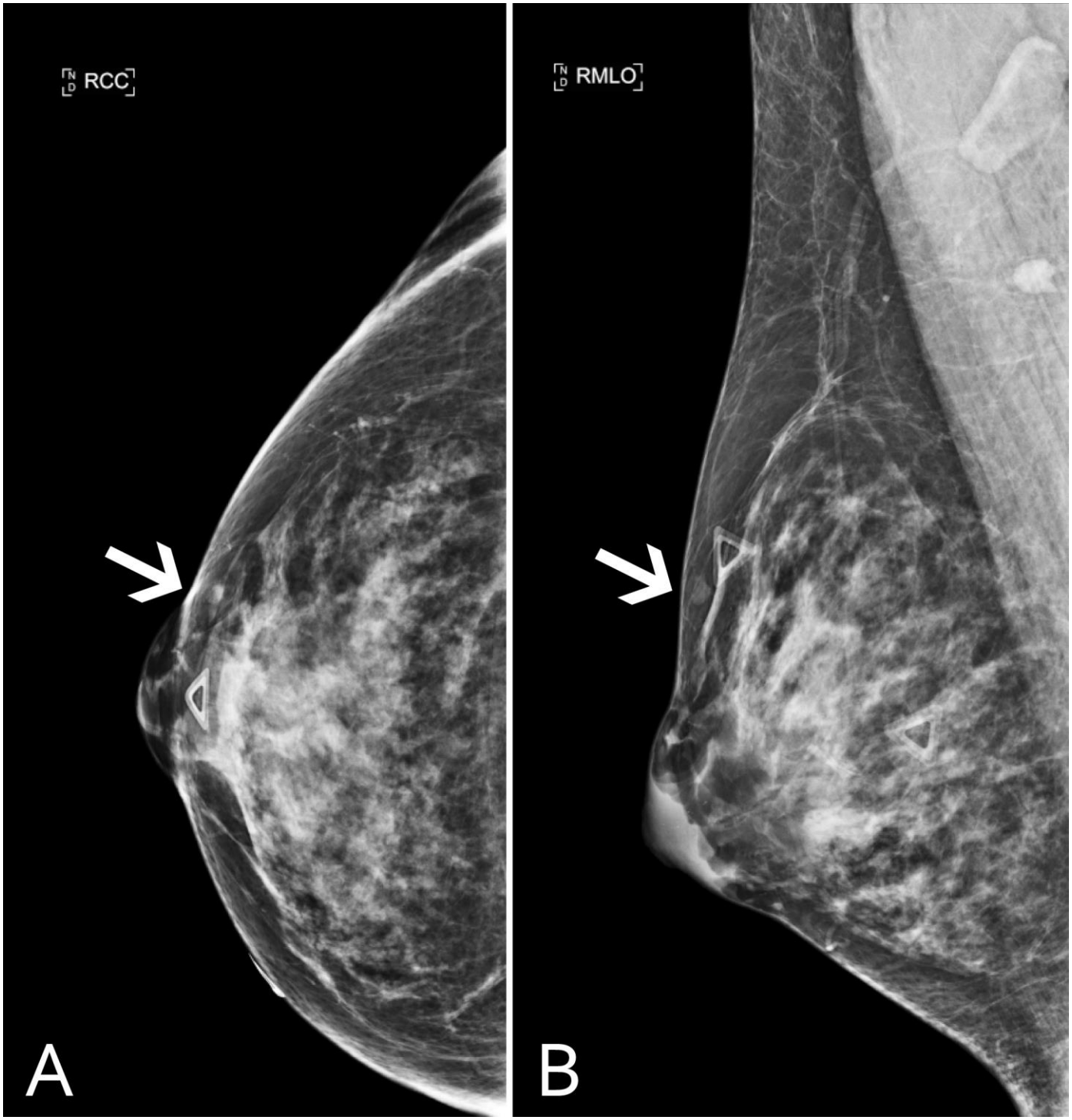
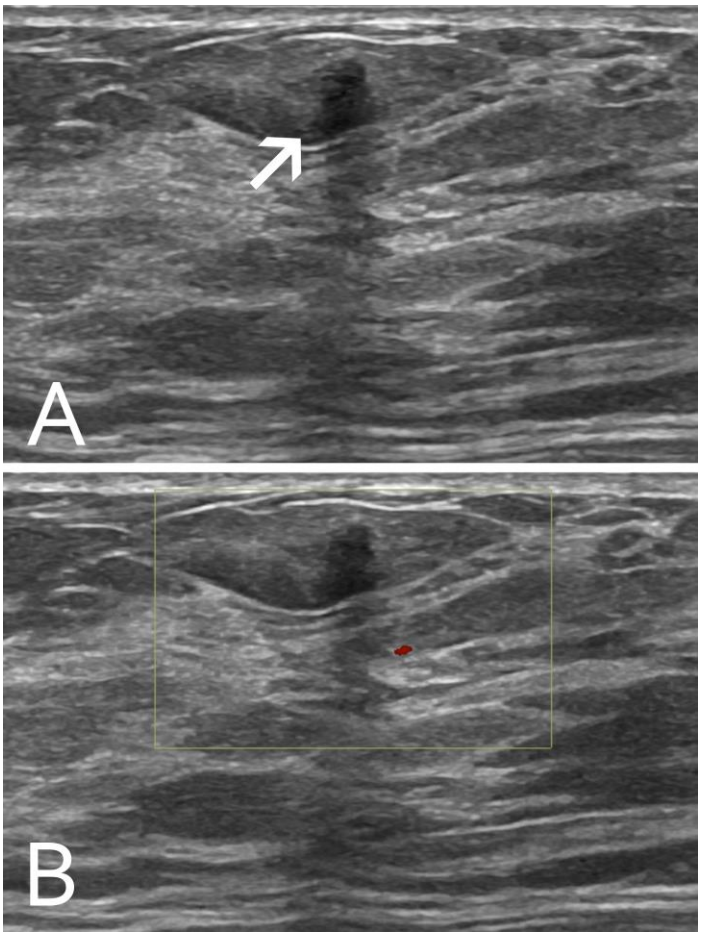


Figure 1: 36 year old male-to-female transgender patient with granulomatous mastitis.
FINDINGS: (A) Mammographic craniocaudal view and (B) mediolateral oblique view of the right breast shows a 5 mm equal density mass in the upper outer breast anterior depth [arrows] which correlates with the palpable marker.
TECHNIQUE: (a) Digital mammogram, craniocaudal view. Tungsten anode; rhodium filter; kVp: 31; mAs: 208. (b) Digital mammogram, mediolateral oblique view. Tungsten anode; rhodium filter; kVp: 31; mAs: 178.



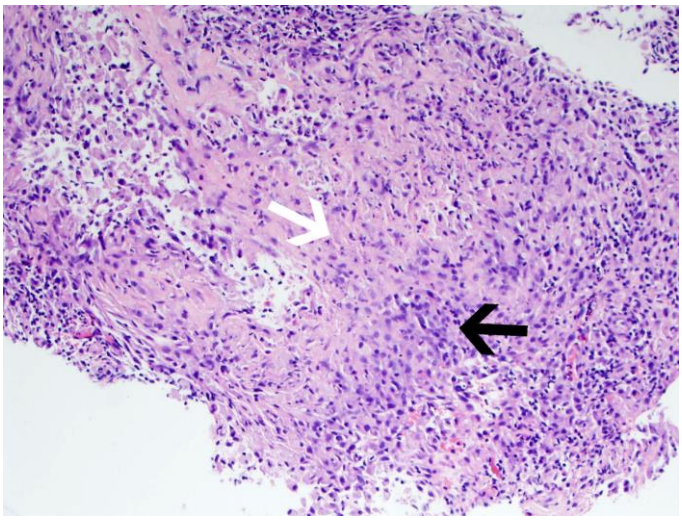


Figure 3 (top): 36 year old male-to-female transgender patient with granulomatous mastitis.
FINDINGS: Histology shows an organized collection of macrophages [white arrow] with surrounding inflammation and giant cells [black arrow], forming granulomas.
TECHNIQUE: Hematoxylin and Eosin stain, 100x magnification.

Figure 2 (left): 36 year old male-to-female transgender patient with granulomatous mastitis.
FINDINGS: (A) Grayscale and (B) Color-doppler ultrasound of the right breast at 11 o'clock shows a heterogeneous, hypoechoic, irregular, non-parallel mass [arrow] with posterior acoustic shadowing.
TECHNIQUE: 15Mhz linear sonographic transducer.

Etiology	Unknown; favor autoimmune
Incidence	0.025%-3% of surgically treated breast disease
Gender ratio	Almost exclusively women
Age predilection	Women of child-bearing age; mean age of presentation of 33-38 years old
Risk factors	Child bearing age, oral contraceptives, recent pregnancy, lactation
Treatment	No clear consensus; surgical wide excision, steroid therapy, methotrexate, colchicine, azathioprine, expectant management
Prognosis	Benign; high rate of recurrence (16-50%)
Findings on Imaging	Mammography – focal asymmetry or mass Ultrasound – heterogeneous hypoechoic lesions often with tubular extensions

Table 1: Summary table of granulomatous mastitis.

	XR	US	MRI
Granulomatous mastitis	- Heterogeneous or extremely dense parenchyma - Asymmetry or irregular masses - Skin thickening - Axillary adenopathy - Calcifications are rare	- Irregular hypoechoic mass usually with hypoechoic tubular extensions - Perilesional echogenicity - Vascularity of surrounding tissues - Fistula formation - Skin thickening	- Heterogeneous segmental T1 hypointense, T2 hyperintense signal - Non-masslike enhancement on postcontrast dynamic T1-weighted -Heterogeneously enhancing irregular lesions with gradual enhancement without washout -Skin thickening and nipple retraction
Acute Mastitis/Abscess	- Asymmetric density, mass, or distortion - Calcifications are rare - Skin and trabecular thickening - Axillary adenopathy	- Increased parenchymal echogenicity - Multiloculated, nonvascular, hypoechoic fluid collections - Skin thickening	- Heterogeneous T2 signal correlating with parenchymal edema - Rim-enhancing irregular mass - Skin and trabecular thickening
Inflammatory breast cancer	- Skin and trabecular thickening - Global asymmetry - Axillary adenopathy - Less commonly multiple masses, calcifications or architectural distortion	- Increased parenchymal echogenicity - Increased diffuse vascularity - Skin thickening - Dilated lymphatics	- Streaky T2 signal correlating with parenchymal edema - Rapid enhancement with delayed washout; enhancing irregular masses, non-masslike enhancement or reticular/dendritic enhancement - Skin thickening and enhancement
Invasive breast carcinoma	- Irregular mass with spiculated or indistinct margins - Architectural distortion - May have calcifications - Axillary adenopathy	- Irregular, hypoechoic vascular mass with indistinct, angular or spiculated margins - Perilesional echogenicity	- Irregular enhancing mass or segmental area of non-masslike enhancement, which demonstrates early washout kinetics (Type 3)

Table 2: Differential diagnosis table for granulomatous mastitis.

ABBREVIATIONS

AFB - acid-fast bacilli
GM - granulomatous mastitis
GMS - Grocott-Gomori methenamine silver
IBC - inflammatory breast cancer
I&D - incision and drainage
MR - magnetic resonance
MtF - male-to-female

KEYWORDS

granulomatous mastitis; transgender; breast; mammogram; ultrasound

Online access

This publication is online available at:
www.radiologycases.com/index.php/radiologycases/article/view/2934

Peer discussion

Discuss this manuscript in our protected discussion forum at:
www.radiolopolis.com/forums/JRCR

Interactivity

This publication is available as an interactive article with scroll, window/level, magnify and more features.
Available online at www.RadiologyCases.com

Published by EduRad

www.EduRad.org