ISSN: 2165-3259

JAOCR

Official Journal of the American Osteopathic College of Radiology

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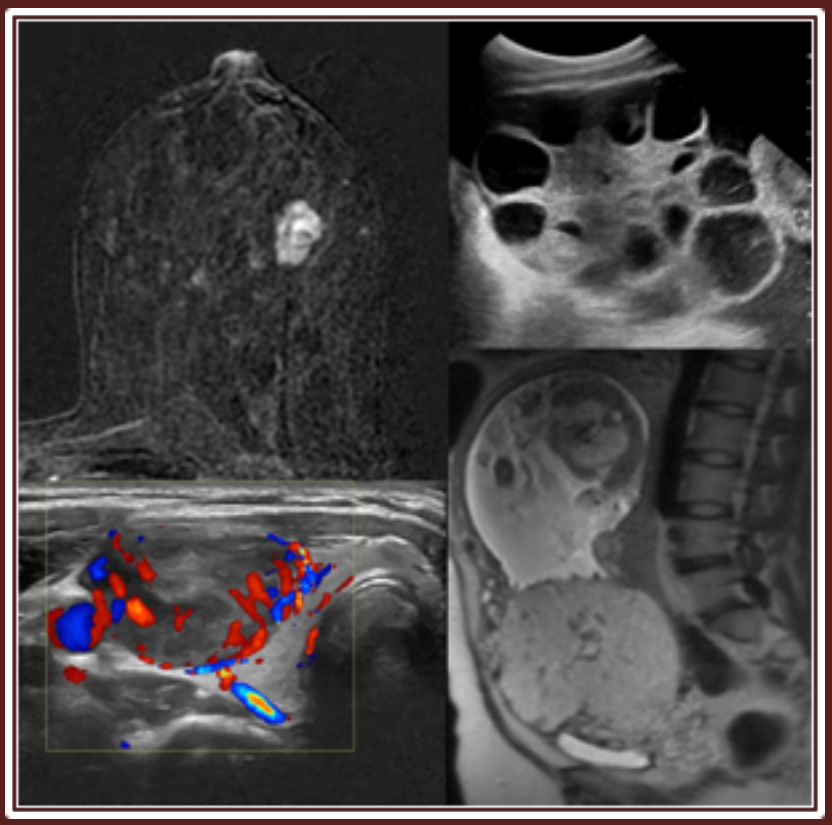

Guest Editor: Chandni Bhimani, D.O.

Editor-in-Chief: Daniel J. Wale, D.O.

April 2019, Vol. 8, Issue 2

JAOCR

Official Journal of the American Osteopathic College of Radiology

Aims and Scope

The Journal of the American Osteopathic College of Radiology (JAOCR) is designed to provide practical up-to-date reviews of critical topics in radiology for practicing radiologists and radiology trainees. Each quarterly issue covers a particular radiology subspecialty and is composed of high-quality review articles and case reports that highlight differential diagnoses and important teaching points.

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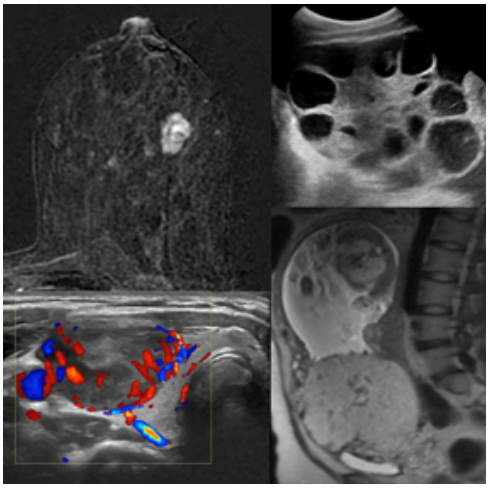

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"Mentoring is a brain to pick, an ear to listen, and a push in the right direction."
John C. Crosby

In this Issue

Chandni Bhimani, D.O.

Breast Imaging Fellow, Department of Radiology, Thomas Jefferson University Hospital, Philadelphia, PA

Thank you for this opportunity William O'Brien, D.O, former editor-in-chief, and thank you Daniel Wale, D.O., current editor-in-chief, for your guidance and support on this issue. A unique dual-institution collaboration between my former radiology residency institution, Cooper University Hospital in Camden, NJ, and my fellowship institution, Thomas Jefferson University Hospital in Philadelphia, PA, where I am a breast imaging fellow, resulted in the production of this Reproductive Imaging issue of JAOCR. The strengths of these two institutions and their esteemed faculty have contributed to the foundation of my early radiology career.

For most women, reproductive years represent a happy and joyful period in their lives. However, pregnancy and postpartum are not without risks and complications that affect not only the livelihood of a young woman but her family as well. Specifically, pregnancy is a vulnerable period in a woman's life, which can lead to significant morbidity and mortality. Imaging evaluation plays a crucial role in evaluation and diagnosis of common disease processes seen during this important time period. This issue includes imaging evaluation of breast, renal, thyroid, genitourinary and obstetrical disease processes encountered during pregnancy and lactation.

My advisors and mentors have pushed me to reach my potential and taught me to give back to those that follow in my footsteps. As such, I have sought out residents from my residency and fellowship institutions as first authors and co-authors for all of the articles in this issue. I would like to express my appreciation and gratitude to all the authors for their time and dedication in creating this issue. I hope that this opportunity will inspire trainees to mentor those that follow them and contribute to the advancement of our field.

I would like to thank everyone who has supported me on this winding training path at Cooper University Hospital and Thomas Jefferson University Hospital, especially Pauline Germaine, D.O., and Robyn Roth, M.D., who have fostered my clinical and research interests in women's imaging. I am fortunate for my roots and will be staying local to serve the South Jersey community as a breast and body radiologist at Atlantic Medical Imaging. I would like to thank my family, particularly my husband, Gautam, for his continued support and patience as I have spent countless hours expanding my clinical and research interests in women's imaging.

Breast Masses in Pregnancy and Lactation

Ida Teberian, M.D.,[1] Chandni Bhimani, D.O.,[1] Maria Sciotto, M.D.,[2] Annina Wilkes, M.D.,[1] Pauline Germaine, D.O.[2]

[1]Department of Radiology, Thomas Jefferson University Hospital, Philadelphia, PA
[2]Department of Radiology, Cooper University Hospital, Camden, NJ

Palpable breast lumps during pregnancy and lactation are a common presenting symptom. It is important to recognize benign masses to avoid unnecessary biopsies while maintaining a high clinical suspicion, as 20% of palpable lumps during this period are malignant.[1]

This article will cover the imaging appearances of various benign and malignant masses that may occur during pregnancy and/or lactation on ultrasound, mammography, and MRI.

Physiologic Changes in the Breast During Pregnancy and Lactation

The breast undergoes physiologic changes during pregnancy and lactation due to hormonal stimulation that increases breast size and water content. These changes manifest clinically as increased nodularity and firmness, making it difficult to pinpoint a new palpable finding on self-breast and clinical exam. The breasts return to their normal baseline state 3 months after lactation has ceased.[2]

When clinical concern arises, imaging is crucial for further evaluation. Ultrasound has the highest sensitivity and should be performed first. Mammography is less sensitive during this time due to the increased parenchymal density, which may obscure suspicious findings. This is most problematic in the late third trimester and during lactation.[3] Radiologists must be aware of the normal sonographic appearance of the breast during pregnancy and lactation. During pregnancy, the breasts demonstrate homogeneous hypoechogenicity. The lactating breast, however, demonstrates diffuse hyperechogenicity, as well as prominent ducts and increased vascularity.[1-3] Contrast-enhanced MRI should be avoided in pregnancy if possible but is acceptable during lactation, although sensitivity will be decreased. Normal lactational tissue demonstrates diffusely increased T2 signal due to the increased water content as well as rapid and plateau enhancement kinetics of breast parenchyma.[2,3]

Breast Masses Unique to Pregnancy and Lactation

Lactating Adenoma

Lactating adenomas are benign masses that arise in response to hormonal changes during pregnancy and lactation. They are common, representing 70% of biopsied masses in this population.[4] Lactating adenomas are similar to fibroadenomas but exhibit unique histologic features, most importantly the lack of both stromal components and myoepithelial proliferation. They are comprised of clusters of secretory lobules whose acini contain abundant secreted material including proteins, lipids and colostrum.[1,3]

Lactating adenomas most commonly arise as a single mass that is palpable and mobile, although they can be multiple and bilateral. They often present during lactation and rarely prior to the third trimester of pregnancy. Uniquely, they can regress spontaneously after return to a nonlactating state.[1]

Lactating adenomas share the same imaging appearance as fibroadenomas, with the most common sonographic appearance being a homogeneously hypoechoic solid mass with circumscribed margins and parallel orientation (**Figure 1**). Like fibroadenomas, they can develop areas of infarction due to rapid growth. They can have hypoechoic or hyperechoic areas due to fat content or lactational hyperplasia, respectively, or anechoic regions representing fluid. Suspicious features are also possible, including posterior acoustic shadowing, predominant hypoechogenicity, irregular shape, and microlobulated or indistinct margins, some of which may be secondary to infarction. When seen

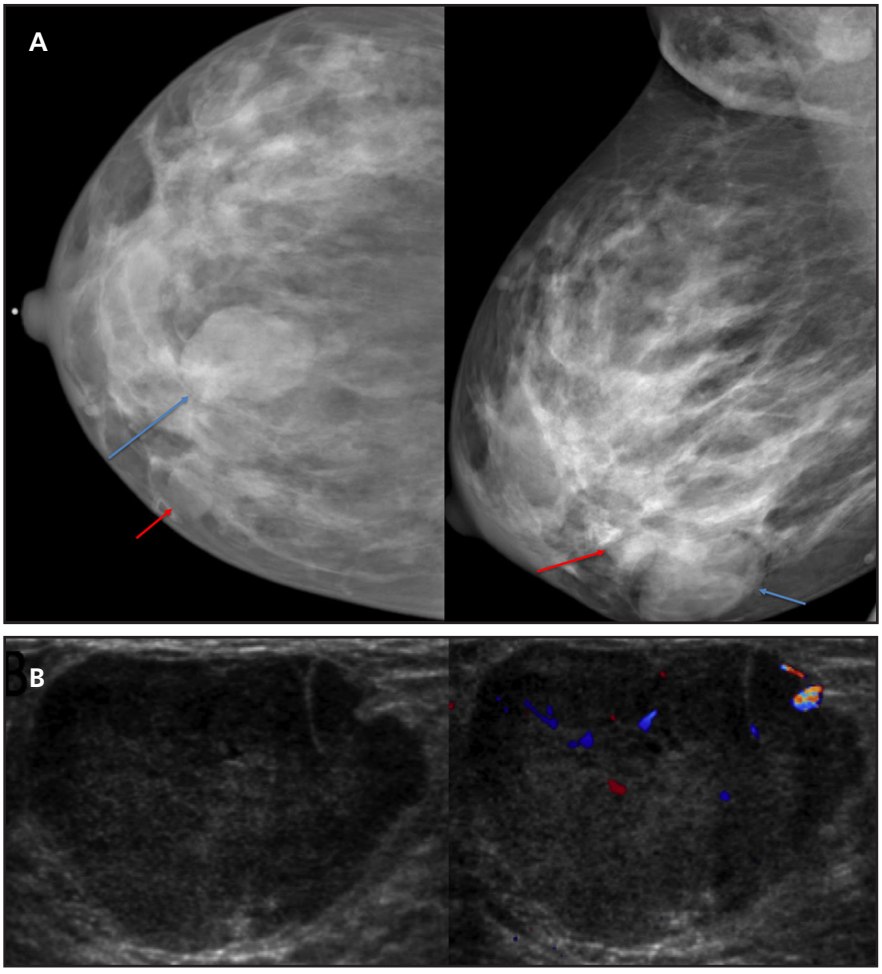

FIGURE 1. *Lactating adenomas in a 37-year-old woman, 35 weeks' pregnant, with palpable lumps in the right breast. (A) CC and MLO mammograms reveal two corresponding circumscribed masses (red and blue arrows). (B) Ultrasound demonstrates circumscribed hypoechoic solid masses with parallel orientation. In this case, core biopsy of both masses revealed lactating adenomas.*

on mammography, they appear as a circumscribed mass with variable density, including low (fat) density, and may also have a fat-fluid level due to colostrum within secretory lobules.[1]

Management is with close imaging surveillance if it appears benign. If it is atypical and without internal fat, biopsy should be performed. Lactating adenomas do not recur after surgical excision.[5]

Galactocele

Galactocele is the most common benign breast mass in a lactating patient, although it more commonly presents after cessation of breastfeeding. It may also present in the third trimester of pregnancy. Galactocele is a retention cyst originating from an obstructed duct.[2] The contents are widely variable, with different proportions of fat, proteins, and lactose possible. Histologically, they demonstrate normal epithelium and myoepithelium.[3] A fibrous wall of variable thickness may be present due to inflammation as inflammation is often the cause of duct obstruction.[1] Galactoceles can also be associated with necrotic debris if there is leakage, which incites an inflammatory reaction resulting in fat necrosis.

Clinically, galactocele often presents as a painless palpable mass discovered after cessation of breastfeeding. If it is

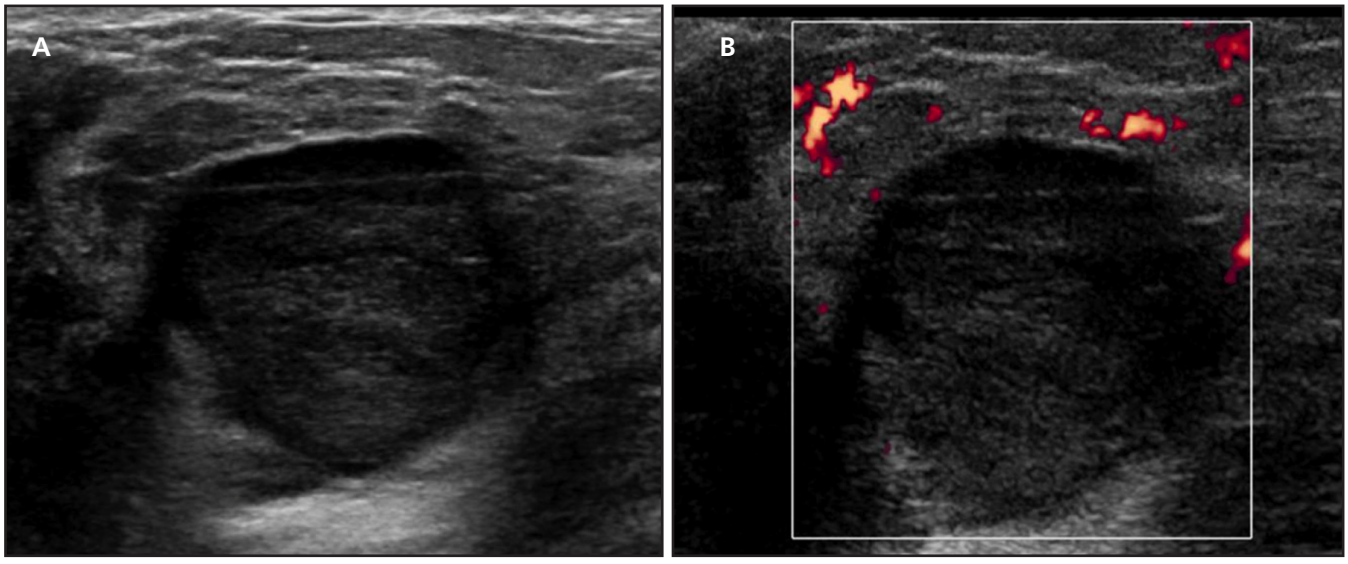

FIGURE 2. *Galactocele in a 30-year-old woman, 6 weeks' postpartum, with a palpable lump in the right breast. (A, B) Ultrasound demonstrates a complicated cyst with a fat-fluid level, posterior acoustic enhancement, and no internal vascularity.*

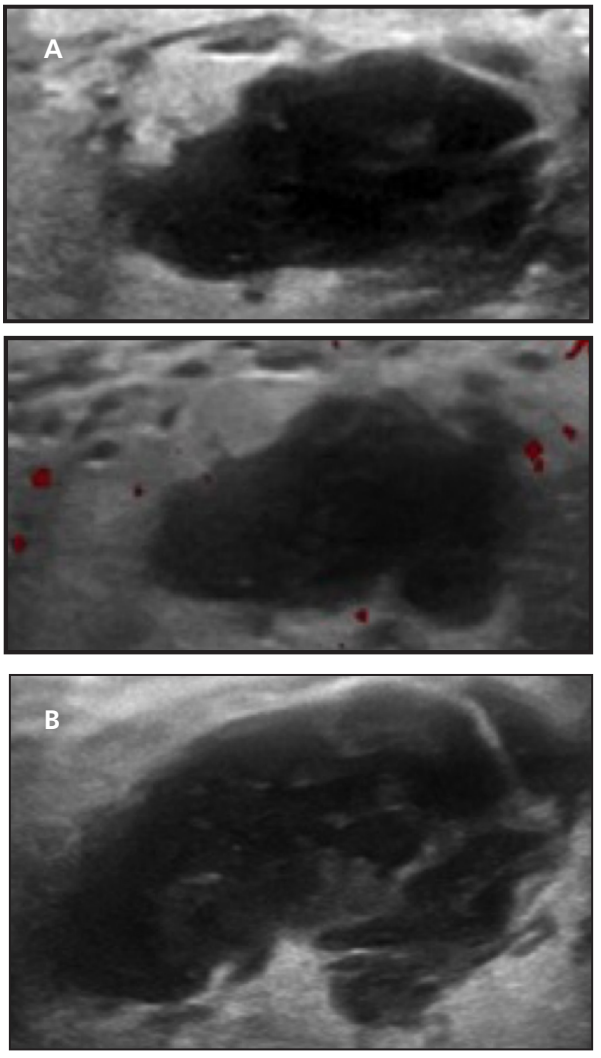

FIGURE 3. *Abscess in a 27-year-old woman, 12 weeks' pregnant, with right breast pain and redness. (A) Gray-scale and power Doppler ultrasound images show a complicated cyst with internal debris and irregular margins, concerning for an abscess. Nipple ring removal was reported by the patient approximately 1-2 months prior to the presentation. The patient was started on antibiotics. (B) Four days later, the patient returned with increased swelling, pain and redness, and ultrasound demonstrated increased size in the presumed abscess. Fine-needle aspiration produced blood-tinged milky fluid which grew Streptococcus Pyogenes Group A.*

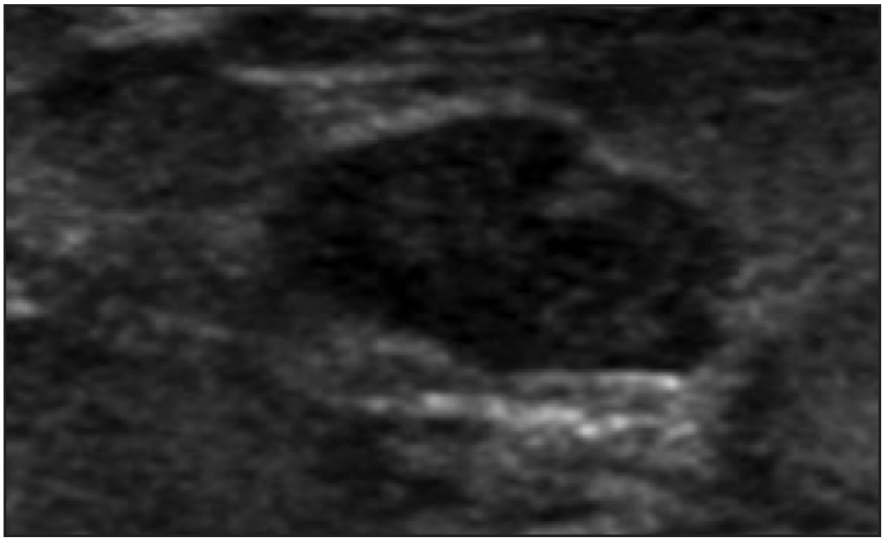

FIGURE 4. *Fibroadenoma in a 33-year-old woman, 6 months' pregnant, presenting for a 6-month follow-up of a cluster of cysts in the right breast. Ultrasound revealed an incidental oval hypoechoic solid mass with parallel orientation and posterior acoustic enhancement. Core biopsy was performed in this patient with a personal history of breast cancer, revealing a fibroadenoma.*

discovered while the patient is still lactating, a history of decreased frequency of breast-feeding is often elicited.[3] Galactoceles can be multiple and bilateral.[4]

The imaging appearance of galactoceles varies depending upon cyst contents. On mammography, it often demonstrates radiolucency, although this depends on the amount of fat present. It can be completely lucent, in which case it is known as a pseudolipoma.[2,5] Alternatively, it may have high density if it contains more viscous fluid. On ultrasound, it most commonly looks like a complicated cyst. An important radiologic sign classically seen on ultrasound is a cyst with a fat-fluid level, which occurs in galactoceles with fresh milk content (**Figure 2A**). This can also be visualized on mammography on the mediolateral (ML) projection. Galactoceles with older milk content have higher viscosity and the fat and water do not separate, resulting in a similar imaging appearance to a fibroadenolipoma.[2] Galactoceles may also appear as a solid mass with circumscribed margins and posterior acoustic enhancement, similar to a fibroadenoma, although a galactocele may also contain echogenic contents representing fat. With superimposed infection, it will appear as a complex cystic and solid mass. It is important to note that vascularity should never be present within the mass (**Figure 2B**).

With classic imaging and clinical features, no further intervention is required as galactoceles may regress spontaneously. Aspiration can be both diagnostic and therapeutic and will yield milky fluid, which may be thickened if performed after lactation has ended. Aspiration of milk must be accompanied by an appropriate clinical and imaging presentation to make the diagnosis, as similar fluid can be aspirated in any mass with lactational changes.[2]

Mastitis and Abscess

Mastitis with or without an abscess occurs more commonly during lactation and is uncommon during pregnancy.

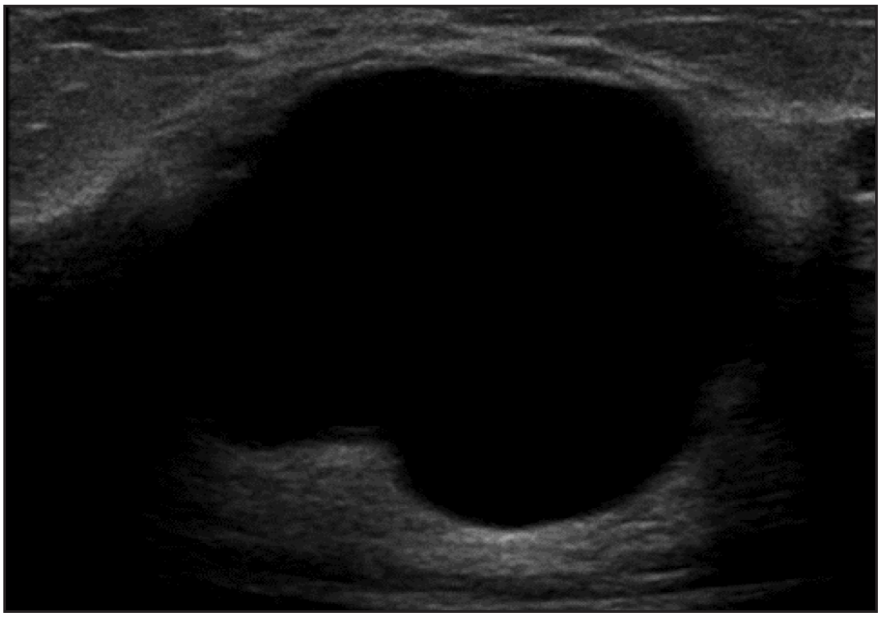

FIGURE 5. *Simple cyst in a 24-year-old woman, 7 weeks' pregnant, who presented with a palpable lump in the left breast. The oval anechoic mass with imperceptible wall and posterior acoustic enhancement correlates to the palpable lump and is consistent with a simple cyst.*

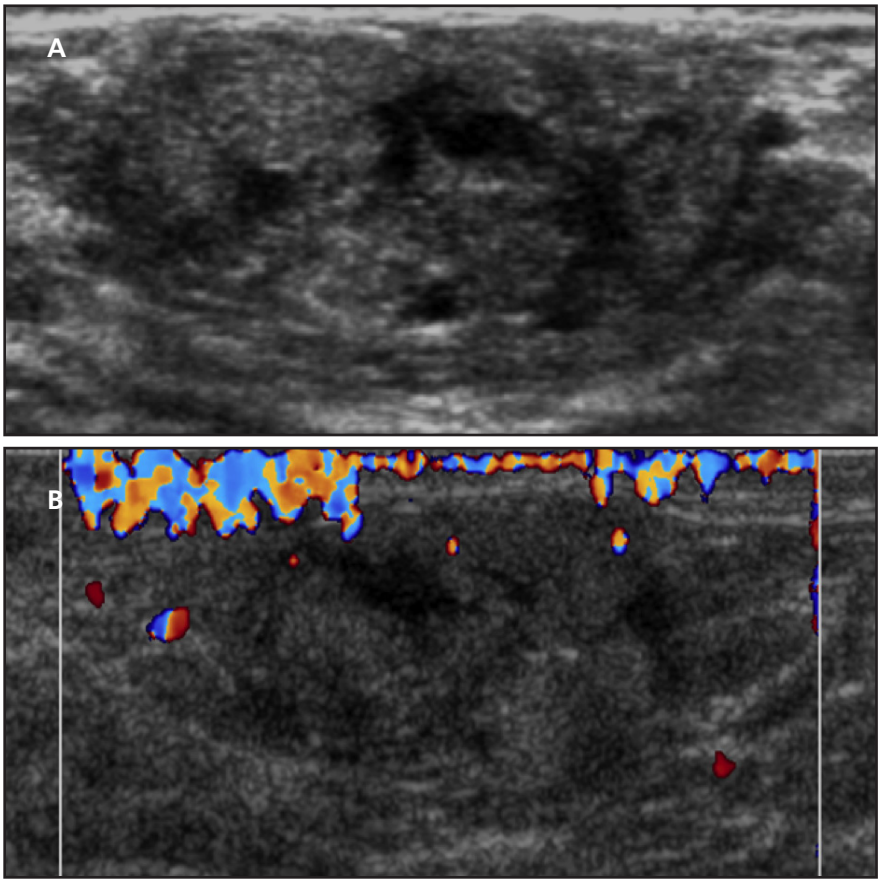

FIGURE 6. *Intraductal papilloma in a 29-year-old woman, 3 months' postpartum and lactating, with a palpable lump in the left breast. Sagittal (A) and Doppler (B) ultrasound images of the left breast demonstrate a complex cystic and solid mass at 10:00, 4 cm from the nipple with internal vascularity. Core biopsy revealed an intraductal papilloma without associated atypia or carcinoma, further confirmed on subsequent delayed excision postcessation of lactation.*

Retrograde dissemination of infectious organisms from the baby's nose or throat occurs through disruption of skin at the nipple areola complex. The most common causative organisms are *Staphylococcus* and *Streptococcus*.[2]

The diagnosis is most often clinical although imaging is indicated if an abscess or malignancy is suspected. Sonographic findings of simple mastitis include inflammation and periductitis. An abscess appears as an irregular hypoechoic or anechoic mass or complex cystic solid mass, with possible fluid or debris and posterior acoustic enhancement (**Figure 3**). Mammography is performed if there is suspicion of cancer, although it is often unrevealing due to increased parenchymal density. There may be skin and trabecular thickening due to edema and possibly a mass if there is an abscess.

Management of breast abscess includes diagnostic and therapeutic aspiration and appropriate antibiotic therapy, as well as surgical debridement if indicated, such as with a persistent or recurrent abscess or if it is > 3 cm.[4] If after appropriate therapy the findings do not resolve, cancer should be suspected and further workup performed.

Breast Masses That May Occur During Pregnancy and Lactation

Other Common Breast Masses in Pregnancy

Fibroadenoma

Fibroadenomas are the most common tumor seen during pregnancy and lactation as they often undergo sudden growth secondary to hormonal stimulation, making them newly palpable. Rapid growth also results in susceptibility to infarction as they outgrow their vascular supply. This manifests clinically as new focal pain with possible adherence to the skin and reactive adenopathy.[1,2]

Fibroadenomas arise in the terminal ductal-lobular unit (TDLU) and contain epithelial and stromal components. Secretory or lactational changes can be observed during pregnancy and lactation, whereas hyalinization, calcification,

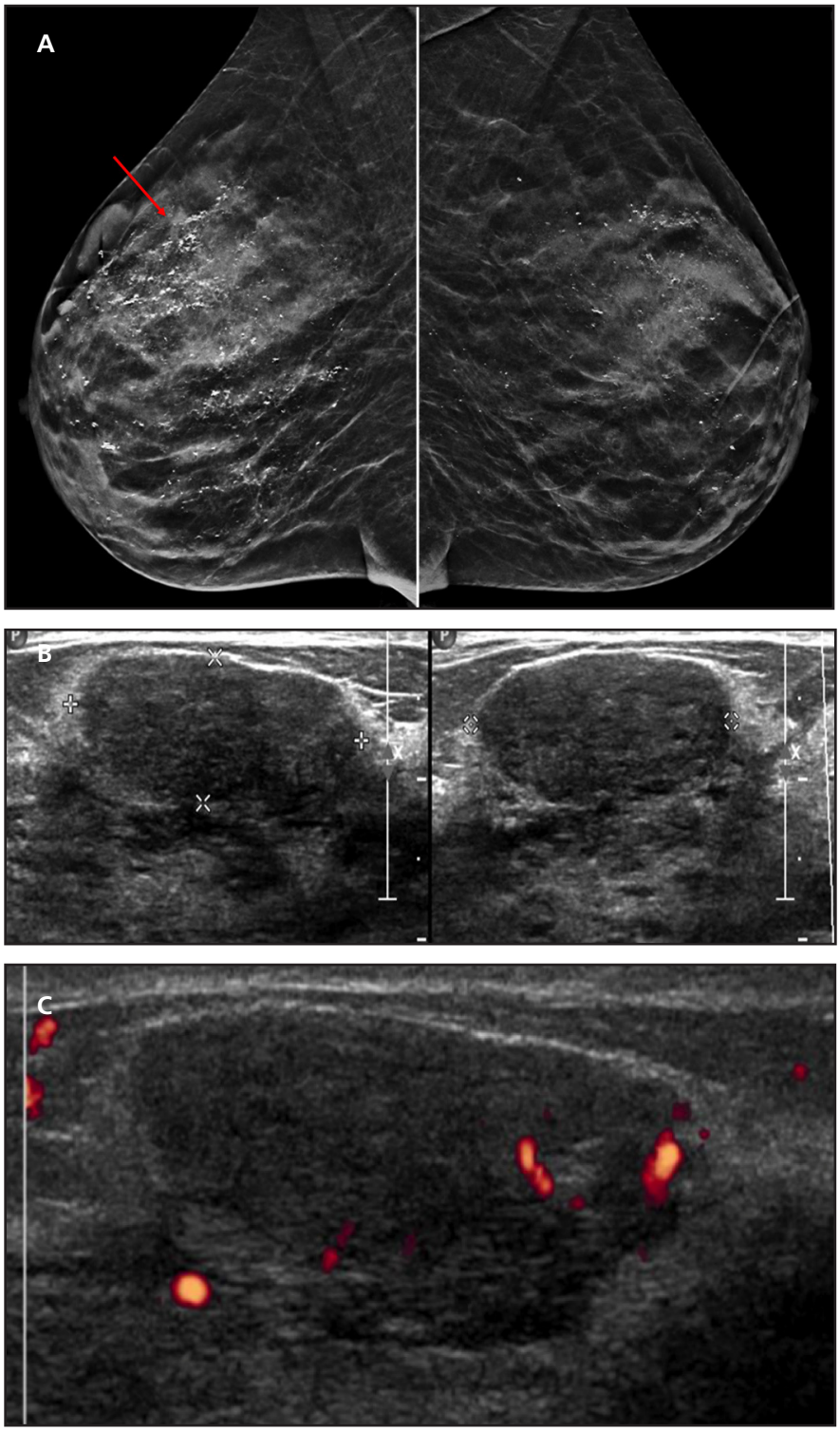

FIGURE 7. *One of the many possible imaging appearances of pseudoangiomatous stromal hyperplasia (PASH) is shown in a 40-year-old nonpregnant, nonlactating woman with a palpable lump in the right breast, increasing in size over time. (A) MLO views of the right breast demonstrate a mass at the 12:00 position, 4 cm from the nipple (red arrow). The patient had recently undergone percutaneous biopsy of the left breast, demonstrating an intraductal papilloma. (B) Ultrasound images of the palpable area in the right breast demonstrate an oval, isoechoic solid mass with circumscribed margins and parallel orientation. Subsequent core biopsy revealed PASH. (C) Mild internal vascularity is present within this mass on power Doppler evaluation.*

and ossification are atypical, classically occurring in older lesions in postmenopausal women.

The imaging appearance is usually identical to fibroadenomas in nonpregnant, nonlactating patients (**Figure 4**). A more complex appearance is possible during pregnancy, with cystic areas and/or prominent ducts, as well as greater vascularity. This may be due to infarction, which can also result in more lobulated margins, more heterogeneous echogenicity, and posterior acoustic shadowing.[1]

Nonpalpable fibroadenomas and those previously present with up to 20% growth in size can undergo close surveillance. Any atypical appearance or new mass should undergo histologic analysis. Diagnosis can be made with fine-needle aspiration (FNA) or core needle biopsy, as discussed below in "Tissue sampling during pregnancy and lactation." It is important to keep in mind that in fibroadenomas with secretory or lactational hyperplasia, milk can be aspirated, and calcifications may be present.[2]

Cysts

Cysts and fibrocystic changes are benign entities that occur with the same frequency during pregnancy and lactation as they do outside of these conditions. They are an important consideration in the differential diagnosis of palpable masses in pregnant and lactating women as they are most common in young premenopausal women.[4]

Cysts form either due to duct obstruction or an imbalance between secretions and absorption. Fibrocystic change represents various benign changes of ducts and stroma, such as adenosis, apocrine metaplasia, and usual ductal hyperplasia. It can present as cyclical breast pain and/or a palpable lump.

Cysts appear as circumscribed, homogeneous masses on mammography. Ultrasound is diagnostic, demonstrating an anechoic, round or oval mass with an imperceptible wall and posterior acoustic enhancement (**Figure 5**). In the case of complicated cysts, it is important to adhere to stringent diagnostic

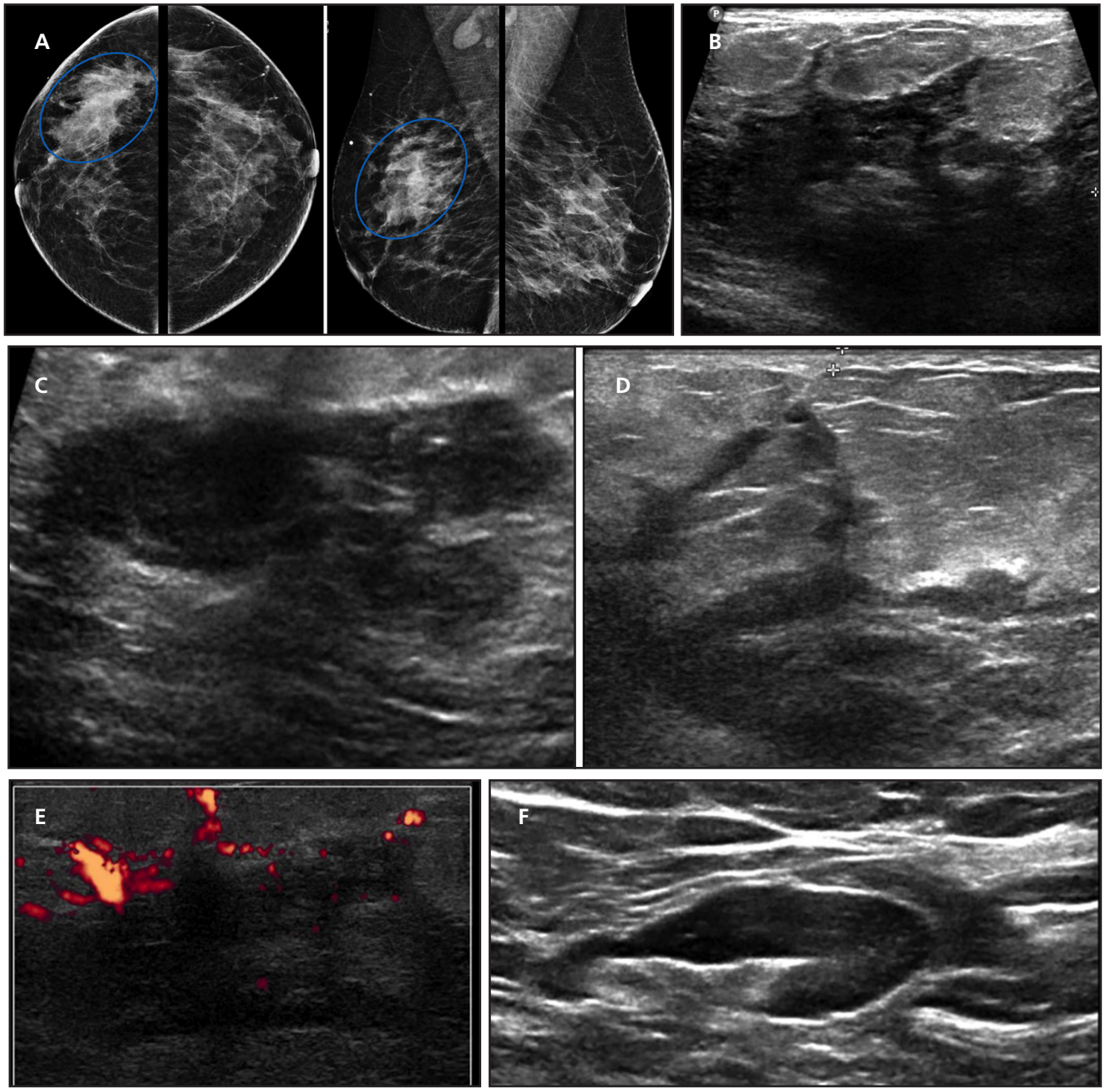

FIGURE 8. *Granulomatous mastitis in a 30-year-old woman, lactating and 2 years postpartum, with a palpable lump in the right breast. (A) Two-view bilateral mammogram reveals a focal asymmetry in the right breast, deep to the BB marker, with associated architectural distortion (blue ovals). (B-F) Ultrasound of the right breast in the area of palpable concern demonstrates a suspicious-appearing hypoechoic area spanning at least 5 cm with internal vascularity. (C) Some areas appear more mass-like than others and (D) there are associated tubular, hypoechoic structures. Mild skin thickening was also noted on the affected side. (F) Ultrasound of the right axilla revealed abnormal-appearing lymph nodes with asymmetric cortical thickening. Subsequent core biopsy of the palpable mass revealed granulomatous mastitis.*

criteria, including round or oval shape, uniform hypoechogenicity or fine internal echoes, circumscribed margins, posterior acoustic enhancement, and lack of a perceptible wall. Management of complicated cysts in pregnancy and lactation includes close surveillance or aspiration, as the differential diagnosis includes galactocele and abscess.[1] The MRI appearance of cysts is a uniformly T2-hyperintense, round or oval, nonenhancing mass.

Clustered microcysts represent a benign sonographic finding most often reflecting either fibrocystic change or apocrine metaplasia and are most common in perimenopausal women.[4] The typical appearance is a mass consisting of a group of 1-7 mm cysts with thin septae and lack of a solid component. They may be round, oval, or microlobulated

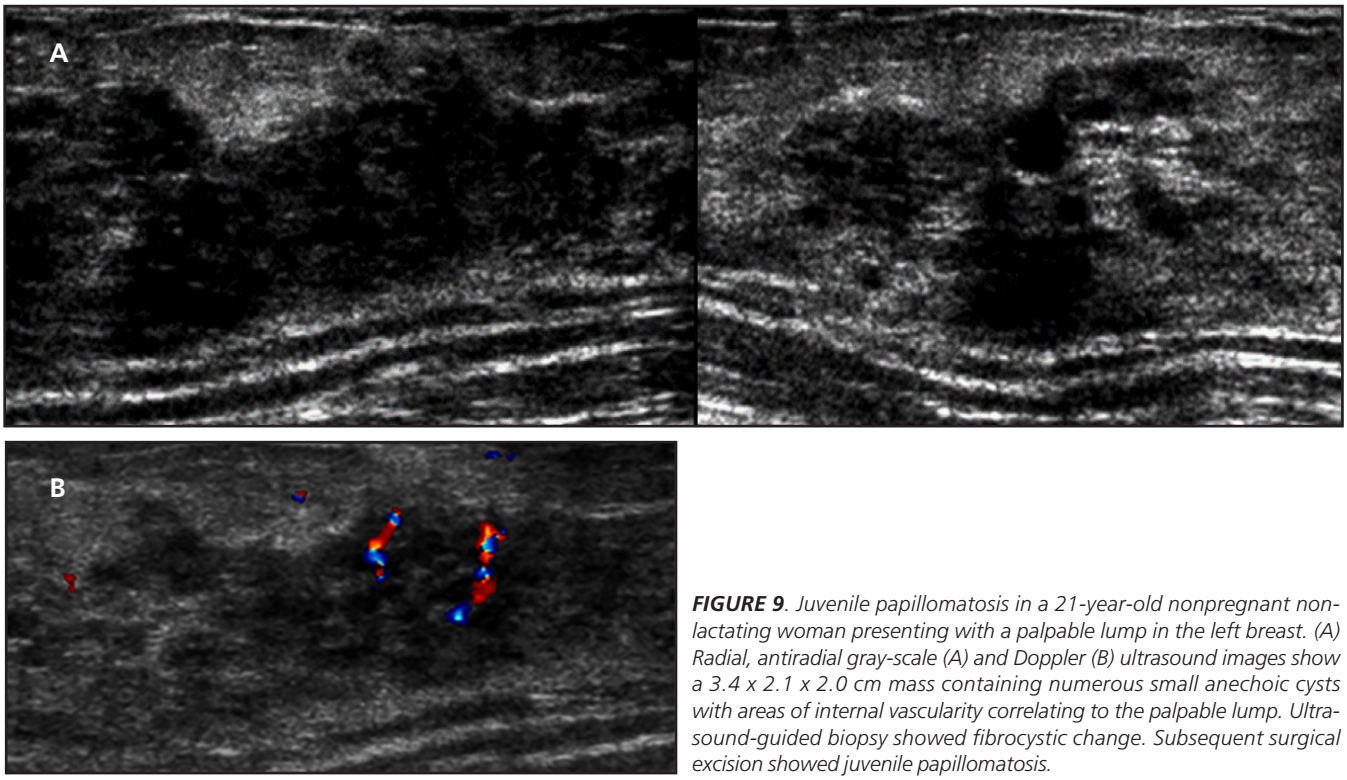

***FIGURE 9**. Juvenile papillomatosis in a 21-year-old nonpregnant nonlactating woman presenting with a palpable lump in the left breast. (A) Radial, antiradial gray-scale (A) and Doppler (B) ultrasound images show a 3.4 x 2.1 x 2.0 cm mass containing numerous small anechoic cysts with areas of internal vascularity correlating to the palpable lump. Ultrasound-guided biopsy showed fibrocystic change. Subsequent surgical excision showed juvenile papillomatosis.*

and have circumscribed margins. They can contain debris as well as milk of calcium. MRI will show T2 hyperintensity with nonenhancing hypointense septations.[4] If there are any atypical features, including a solid component, indistinct margins, rapid growth, or suspicious calcifications, biopsy should be performed.

Fibrocystic change has various sonographic appearances, including complicated cyst and clustered microcysts. Less commonly, it can appear as a thick-walled cystic mass with posterior acoustic shadowing due to fibrosis. On mammography, it is often occult but may be seen as a focal asymmetry or circumscribed mass similar to a cyst. MRI can show cysts, rim-enhancing cysts, scattered enhancing foci, or focal or regional nonmass enhancement.[4]

FNA can be performed for a symptomatic cyst for therapeutic relief. If cyst diagnosis is not certain based on imaging features, FNA can be performed to resolution to confirm that the finding is a cyst. If the cyst does not fully aspirate or a solid component persists, core biopsy should be considered.

Other Breast Masses Not Unique to Pregnancy

Intraductal Papilloma

Intraductal papilloma is a benign tumor representing papillary proliferation of ductal epithelium surrounding a fibrovascular stalk. Papillomas occur most often in women ages 30 to 50 years but are rare, accounting for 0.7% to 4% of solid breast lesions.[4] It can be solitary or multiple, with the solitary type usually in the central and retroareolar breast and in older patients, compared to multiple papillomas, which are usually peripheral and in younger patients.[4,6] They confer a slightly elevated risk of breast cancer, with a greater risk associated with multiple papillomas. The elevated risk is equal in both breasts.[7] Additionally, papillomas may be associated with atypia and ductal carcinoma in situ (DCIS), which are also more common with multiple papillomas.

Solitary papillomas present with bloody or nonbloody nipple discharge in 75% of cases. Bloody discharge occurs in cases of infarction and necrosis.[4,5] Multiple papillomas can present as palpable masses or with nipple discharge.

Ultrasound is more sensitive than mammography in detecting papillomas, which classically appear as a complex cystic and solid mass, representing growth within a duct (**Figure 6**). They may also appear as solid masses, similar to fibroadenomas. A feeding vessel may be identified, but it is important to keep in mind that lack of flow does not exclude the diagnosis.[4] This is especially important in pregnant and lactating women, as inspissated material within a focally dilated duct can mimic a papillary mass. Mammography may demonstrate a cylindrical, round, or oval mass, a focal asymmetry, or calcifications, which are present in 25%.[7] MRI may depict a dilated duct containing an oval, enhancing mass, although irregular or spiculated margins and heterogeneous enhancement are also possible. The kinetic enhancement patterns are variable.[4] MRI has high sensitivity for detecting papillomas since they are typically vascular.

Diagnosis is made by core biopsy. The differential diagnosis includes papillary carcinoma, which is rare and most often occurs in postmenopausal

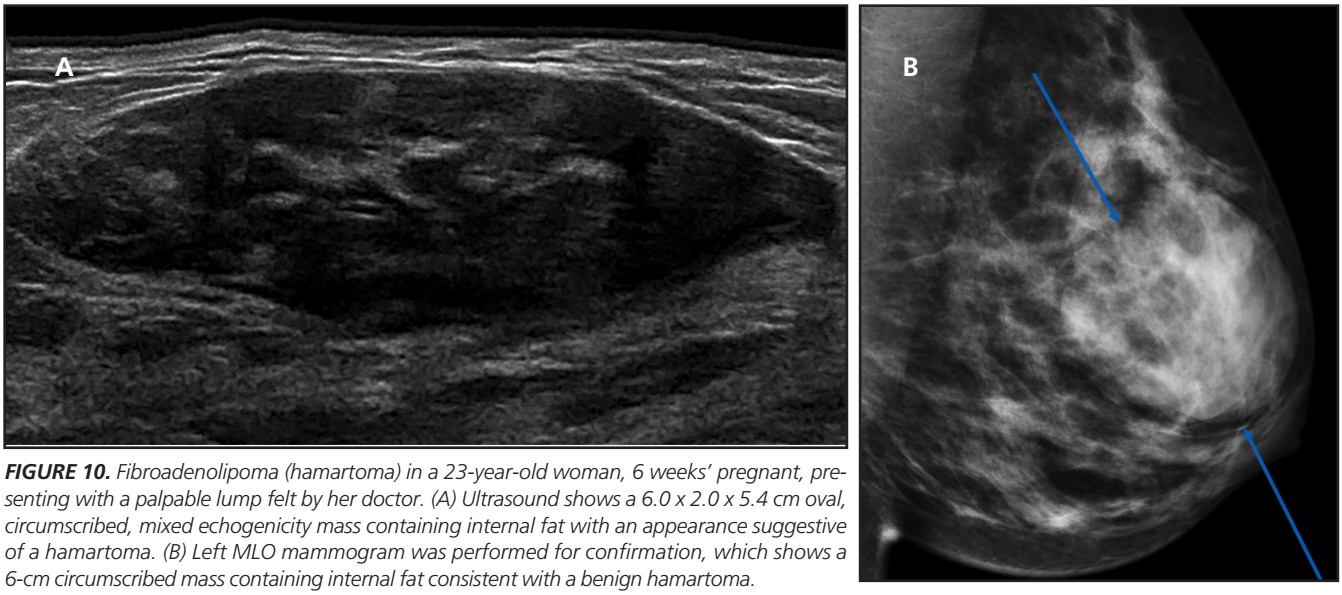

FIGURE 10. *Fibroadenolipoma (hamartoma) in a 23-year-old woman, 6 weeks' pregnant, presenting with a palpable lump felt by her doctor. (A) Ultrasound shows a 6.0 x 2.0 x 5.4 cm oval, circumscribed, mixed echogenicity mass containing internal fat with an appearance suggestive of a hamartoma. (B) Left MLO mammogram was performed for confirmation, which shows a 6-cm circumscribed mass containing internal fat consistent with a benign hamartoma.*

women, and invasive ductal carcinoma with central necrosis and/or duct extension. Benign papillomas can undergo surveillance or be surgically excised. When associated with symptoms or atypia on pathology, they are likely to be excised.

Pseudoangiomatous Stromal Hyperplasia (PASH)

Pseudoangiomatous stromal hyperplasia (PASH) is an idiopathic benign proliferation of nonspecialized stroma separating breast lobules and ducts, which contains spindle cells that form clefts or spaces mimicking vascular spaces. This mesenchymal proliferation can be found as a microscopic focus or can form a mass, which can be palpable. PASH occurs in premenopausal women as it is hormone-sensitive. It is more often found microscopically in older patients and is rarely palpable in this population.[5,8] Although benign, PASH is associated with other benign or malignant masses in 23% of cases.[8]

PASH has no specific imaging features and often resembles other masses, both benign and malignant (**Figure 7**). When it forms a mass, it is usually circumscribed with a round or oval shape and variable size. Mammography may depict a focal asymmetry or mass with no associated calcifications. If calcifications are present, they are due to a separate associated diagnosis. The mass is hypoechoic on ultrasound, usually with smooth margins and variable posterior sound transmission. MRI is equally nonspecific, demonstrating a mass or nonmass enhancement with variable T1 and T2 signal properties, although benign type 1 kinetics are most common. A suggestive MRI appearance is a mass containing T2-hyperintense slit-like spaces and cystic components.[8]

Due to its nonspecific imaging appearance, PASH is a pathologic diagnosis. Clinically and radiologically it mimics fibroadenomas. Histologically, it can mimic low-grade angiosarcoma, which occurs predominantly in young women. Diagnosis of low-grade angiosarcoma can be made by identifying red blood cells within true vascular spaces and testing for endothelial cytologic markers.[8]

Treatment of PASH is controversial although many agree that surgical excision is not necessary if pathology is concordant, in which case close surveillance is recommended.[4,8] Masses can grow over time and lead to discomfort or pain, in which case they are excised. Excision is also recommended in patients with a strong family history of breast cancer. Complete surgical excision is often performed in asymptomatic, average-risk patients due to the possibility of local recurrence and associated atypia, carcinoma in situ, or invasive carcinoma.[8-10]

Granulomatous Mastitis

Granulomatous mastitis is a very rare idiopathic inflammatory disease that has an association with pregnancy, with most patients presenting at a young age and usually within 5 years of pregnancy.[2] Clinical presentation may be with solitary or multiple firm palpable masses and possible associated lymphadenopathy or a more diffuse process.[11] There is no predilection for a specific location, although the subareolar breast is often spared.[2,4]

Mammograms are often normal but the most common finding is a focal asymmetry (**Figure 8A**).[2] It can also present as a mass with variable features. Ultrasound may show the classic appearance of multiple clustered tubular hypoechoic lesions, possibly with an associated hypoechoic mass (**Figures 8B-F**).

The diagnosis is one of exclusion as the histologic features are nonspecific, consisting of a noncaseating, nonvasculitic granulomatous reaction centered around breast lobules. The differential diagnosis for this is large and includes fungal and tuberculous infections, sarcoidosis, and a granulomatous reaction to carcinoma.[2,4]

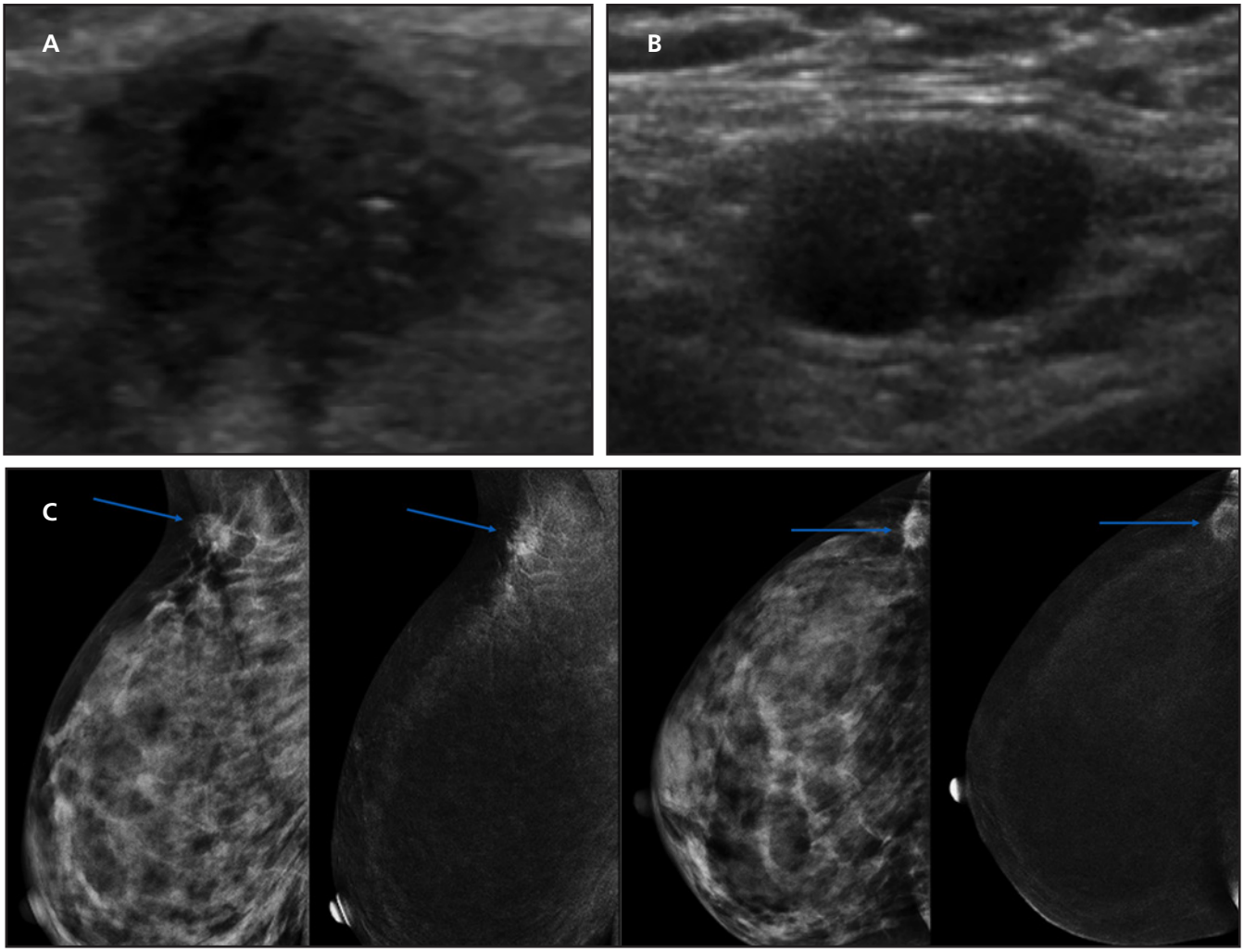

FIGURE 11. *Invasive ductal carcinoma in a 29-year-old woman, 2 months' postpartum, with a palpable right axillary lump felt by her gynecologist. (A, B) Ultrasound of the right axilla shows a hypoechoic, irregular solid mass in the axillary tail (A) as well as abnormal axillary lymph node, with loss of the fatty hilum (B). (C) Contrast-enhanced spectral mammography MLO and CC low-energy and subtraction images performed on the day of biopsy reveal a corresponding spiculated mass in the axillary tail. Core biopsy revealed invasive ductal carcinoma, ER/PR - and Her-2/neu +.*

Prognosis is good despite the possibility of local recurrence with surgical excision and corticosteroid therapy. If an organism is isolated, antibiotic therapy can be effective.[2,4,11]

Juvenile Papillomatosis

Juvenile papillomatosis is a very rare benign proliferative disorder that occurs more frequently during pregnancy and lactation as it is affected by hormonal stimulation. It consists of multiple cysts and dilated ducts within a dense fibrous stroma and clinically presents as a firm, mobile mass often at the periphery of the breast, mimicking fibroadenomas.[12] It is associated with increased risk of breast cancer, which may be concurrent with the diagnosis in 5% to 15% of cases and is considered a marker for familial breast cancer as 33% to 58% of patients have a positive family history.[9,12]

Ultrasound classically demonstrates an ill-defined hypoechoic mass comprised of multiple small anechoic cysts, often peripherally located (**Figure 9**). Mammograms are nonspecific and often negative but may show microcalcifications or an asymmetry. The MRI appearance is a lobulated mass containing small internal cysts with marked contrast enhancement with benign-type kinetics.[9,12]

Treatment is by surgical excision with wide margins as local recurrence is a possibility and because of the possible association with malignancy. Annual clinical surveillance after excision is recommended, as well as surveillance of family members.

Fibroadenolipoma (Hamartoma)

Fibroadenolipomas are benign masses containing glandular, stromal, and adipose tissue, the three components of a normal breast. They may occur at any point in a woman's life, including pregnancy and lactation, although there is no predilection for a certain physiologic state. They may present as palpable, soft, painless lumps.

Imaging by mammography and ultrasound depicts characteristic findings.

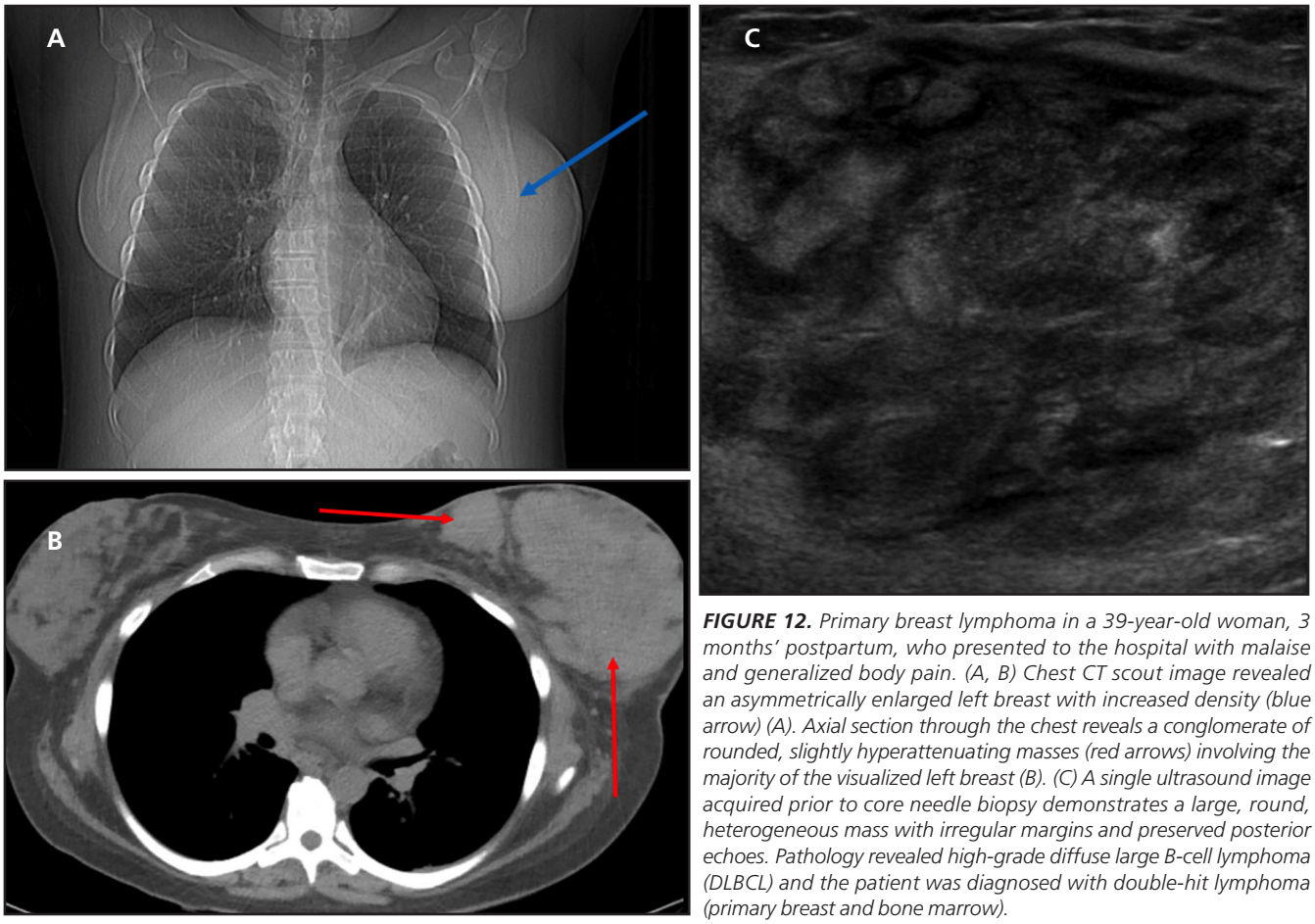

FIGURE 12. *Primary breast lymphoma in a 39-year-old woman, 3 months' postpartum, who presented to the hospital with malaise and generalized body pain. (A, B) Chest CT scout image revealed an asymmetrically enlarged left breast with increased density (blue arrow) (A). Axial section through the chest reveals a conglomerate of rounded, slightly hyperattenuating masses (red arrows) involving the majority of the visualized left breast (B). (C) A single ultrasound image acquired prior to core needle biopsy demonstrates a large, round, heterogeneous mass with irregular margins and preserved posterior echoes. Pathology revealed high-grade diffuse large B-cell lymphoma (DLBCL) and the patient was diagnosed with double-hit lymphoma (primary breast and bone marrow).*

On mammography and ultrasound both fat and parenchymal densities are seen within a circumscribed mass, often termed a "breast within a breast" appearance (**Figure 10**). Similar to other benign masses during pregnancy and lactation, growth and/or infarction can occur, resulting in atypical features.[1] With atypical sonographic features, mammographic demonstration of fat density can be helpful. Ultimately, biopsy must be performed if there is any uncertainty.

Breast Cancer

Pregnancy-associated breast cancer (PABC) is defined as breast cancer diagnosed during pregnancy or within 1 year of childbirth. It is rare, occurring in 1 out of 3,000 to 10,000 pregnancies and constituting 3% of all breast cancers.[2,4] It accounts for 6% to 10% of all cancers in women under 40, with the average age of onset at 34 years old.[1]

Patients usually present in the postpartum period, with 20% occurring during pregnancy.[1] Clinical presentation is usually with a large palpable mass and lymphadenopathy (**Figure 11**). Patients may also present with locally advanced disease, manifesting as swelling, erythema, and enlargement of the breast. The disease is more advanced at presentation compared to nonpregnancy-associated breast cancer in women of the same age. Tumors are more commonly high-grade, more than half present with metastatic lymphadenopathy, and inflammatory cancer is more common. Interestingly, approximately one-third of malignancies occur in high-risk women.[1]

Imaging features are similar to nonpregnancy-associated malignancy and can be benign-appearing, typical of high-grade tumors, demonstrating posterior acoustic enhancement on ultrasound.[1] Mammography is performed as it depicts calcifications, present in up to 55% of cases,[2] and may show multifocal or multicentric disease.

Treatment during pregnancy and lactation has some important considerations. Chemotherapy can be administered during the second and third trimesters with the primary fetal risk being prematurity. Radiation and hormone therapy are contraindicated during pregnancy.[1] Surgery can usually be performed at any point during pregnancy, although waiting until after the first trimester may be appropriate in certain cases.

Lymphoma

Primary breast lymphoma (PBL) is very rare, representing 0.1% of breast cancers, and occuring mostly in women in their fifth and sixth decades.[4,13] It is a form of non-Hodgkin lymphoma (NHL) and most often of B cell lineage. Burkitt lymphoma of the breast

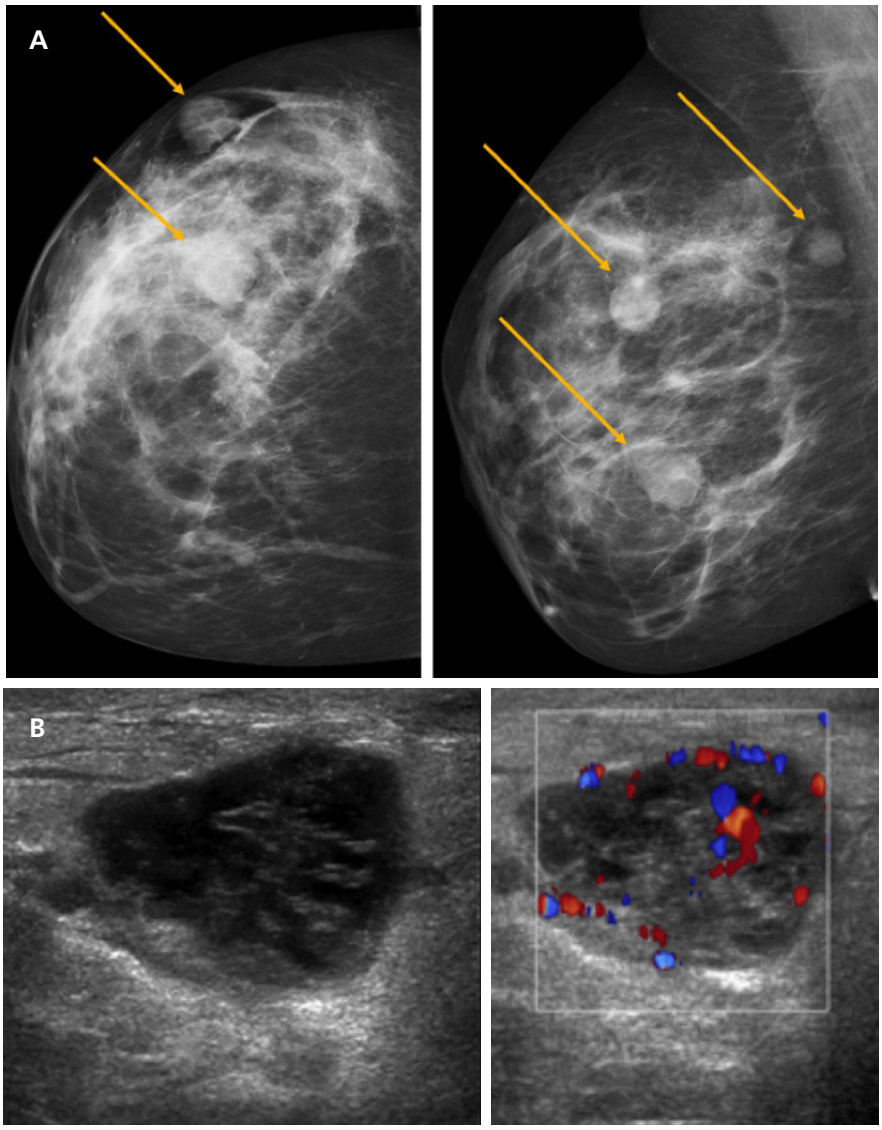

FIGURE 13. *A 43-year-old nonpregnant woman with a history of melanoma presented with a palpable right breast mass. (A) On the mammogram are multiple right breast masses (orange arrows). (B) A representative ultrasound image of the largest right breast mass shows a 2.3 x 2.3 x 1.6 cm heterogeneous vascular mass. This mass was biopsied with results of metastatic/recurrent melanoma.*

(BLB) is a very rare B-cell NHL subtype, which can be endemic, occurring in young African patients, or sporadic, occurring in Europe and the US. The sporadic form is most common and has been associated with pregnancy and the postpartum period, sometimes referred to as pregnancy-related Burkitt lymphoma.[2]

Patients with PBL often present with either a discrete palpable, painful mass or diffuse thickening.[4,14] There is no skin or nipple retraction or nipple discharge and patients rarely experience typical B symptoms (fever, weight loss, and night sweats). There can be diffuse breast enlargement with edema, mimicking inflammatory breast cancer. BLB often causes massive enlargement of both breasts.[2] It is aggressive and infiltrative, causing increased parenchymal density. Findings elsewhere in the body include enlargement of both ovaries and other abdominal organs. Peripheral lymph nodes are rarely involved.[2]

Imaging is nonspecific. A solitary mass is more common than multiple masses, which only occur in 9% of cases and is more common in secondary breast lymphoma (SBL).[13] Mammography may be negative or may show masses or global asymmetry. Mass margins can be indistinct or circumscribed. There are no associated calcifications or architectural distortion. Global asymmetry is seen in one-third of patients and is often associated with high-grade lymphoma.[2,13] There are often associated enlarged axillary lymph nodes. Ultrasound is nonspecific and variable, often demonstrating a round or oval hypoechoic mass with circumscribed or indistinct margins and variable vascularity and posterior acoustic properties, although up to 64% have hypervascularity and up to 75% have posterior enhancement (**Figure 12**).[13] There are often overlying skin changes as it is spread through the lymphatics.[14] Lymphoma on MRI is irregular with mild-to-marked heterogeneous enhancement and restricted diffusion.

PBL is aggressive with high relapse rates, occurring in the CNS in 20% of patients.[13] Treatment is primarily with chemoimmunotherapy and radiation, with surgical treatment offering no benefit.[13,15] Pregnancy-related BLB often spreads rapidly, has a poor prognosis, and can be easily misdiagnosed without adequate immunophenotypic or chromosome analysis.[2,16] Interestingly, it has also been known to spontaneously regress after cessation of lactation.[2]

Metastatic Disease

Metastases to the breast are rare although they are the first manifestation of the primary malignancy in up to 50% of cases.[14] The most common secondary breast malignancies are lymphoma, melanoma, lung and ovarian cancer, and sarcomas.[4] They can present as rapidly growing, painless masses but most are asymptomatic.[17] Prognosis is poor with median survival of 10 months.[18]

Metastases that have spread hematogenously present as masses, whereas those with lymphatic spread result in more diffuse findings similar to lymphoma. Solitary masses are more common, but metastases are more likely to be multiple and bilateral than primary

breast cancer (**Figure 13**). They classically lack signs of a desmoplastic reaction (spiculation, skin/nipple retraction). They are most often in areas of rich blood supply, including the upper outer quadrant, superficial subcutaneous tissue, and edges of breast parenchyma.[14,18] Masses are usually round and circumscribed and rarely cause distortion or contain calcifications. Calcifications can be found with certain malignancies, such as ovarian cancer. Mammographically, the masses are usually high-density with indistinct or microlobulated margins. Most masses are hypoechoic or heterogeneous but can be hyperechoic. They often have posterior enhancement and posterior shadowing is uncommon. Vascularity is variable and depends on the primary tumor.[18] Lymphatically spread malignancy will appear as diffuse heterogeneously hyperechoic adipose and glandular tissue with skin thickening and adenopathy. Although it mimics inflammatory breast cancer, there is no associated mass. MRI will often show T1 and T2 isointensity except for melanoma, which will be T1-hyperintense. Metastases often demonstrate rapid homogeneous enhancement with plateau or washout kinetics.[4,14,17,18]

Tissue Sampling During Pregnancy and Lactation

FNA and core needle biopsy are options for tissue sampling. Core needle biopsy has a high sensitivity and specificity, allowing for a more definitive and confident diagnosis. Core needle biopsy also allows for ancillary testing such as for immunochemistry for estrogen and progesterone receptors in a malignancy, which would not be possible in the setting of FNA; this would be especially important in a BIRADS 4C or BIRADS 5 finding.[22,23]

Due to increased vascularity in pregnancy, there is a slightly higher risk of bleeding and infection. Subcutaneous lidocaine has no known harmful effects to the fetus and is safe to use during pregnancy and lactation.[7]

Milk fistula is rarely a complication of core needle biopsy. Using an oblique track from skin surface to the target for biopsy can help decrease the incidence of milk fistula. If it occurs, it usually resolves on its own in several weeks. If it does not resolve, it may be necessary to suppress lactation to close the fistula.[22,23]

Conclusion

Palpable lumps can be a diagnostic challenge during pregnancy and lactation, both clinically and radiologically. Radiologists must be aware of the appearance of normal physiologic changes as well as the various entities that may present in this population. Biopsy during pregnancy and lactation carries greater risk of bleeding, infection, and fistula formation and can be avoided with adequate knowledge of the diagnostic imaging signs of common benign diagnoses. It is equally imperative to be aware of atypical findings and proceed to biopsy when they are present, however, as pregnancy-associated malignancy carries a poor prognosis that worsens with delayed diagnosis.

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Fibroadenoma: From Imaging Evaluation to Treatment

Kimberly Klinger, M.D., M.S.H.A., Chandni Bhimani, D.O., Jason Shames, M.D., M.B.S., Alexander Sevrukov, M.D.

Department of Radiology, Thomas Jefferson University Hospital, Philadelphia, PA

Background and Epidemiology

Fibroadenoma is the most common benign breast tumor in women younger than age 30. They present most frequently between ages 20 and 50 with peak incidence reported at 20 to 24 years.[1] They account for 68% of all breast masses and a large proportion of breast biopsies.[2]

Fibroadenomas most commonly present as a single, painless, firm, mobile mass, but can be multiple in up to 25% of patients (**Figure 1**).[2] There is a wide spectrum of associated symptoms, from asymptomatic to extremely painful and cosmetically distorting.

Risk factors for fibroadenoma include age < 35 years, history of benign breast disease, and breast self-examination.[2] The incidence of fibroadenoma has also been shown to directly correlate with body mass index (BMI), with peak incidence seen with BMI 25 to 29.9 kg/m.[2] Increased parity and the use of oral contraceptives appear to decrease fibroadenoma risk.[2]

Pathophysiology and Natural History

Fibroadenomas arise from the lobular stroma of the terminal duct lobular unit. They are a proliferation of epithelial and stromal components, likely related to estrogen. Over time, if left in situ, they undergo hyalinization of the stromal component with regression of the epithelial component.[1]

They are hormone-responsive masses and may undergo cyclic changes in size and symptoms with menses. As such, they increase in size during pregnancy and lactation and are the most common breast tumor diagnosed during pregnancy and the peripartum period.[3] Upon hormone withdrawal during menopause, fibroadenomas commonly involute.

The natural history of fibroadenomas varies from patient to patient with some remaining stable, others demonstrating growth, and others regressing. Most commonly, fibroadenomas decrease in size over time as they lose cellularity. Calcifications can form within the hyalinized or necrotic stroma of involuting fibroadenomas, classically described as coarse, "popcorn-like" calcifications.[4] Malignant transformation of fibroadenomas is rare, occurring in less than 0.3%.[2]

Classic Imaging Features of Fibroadenoma

Mammogram

Fibroadenomas are oval, or less frequently round, equal density masses on mammogram with a circumscribed or obscured margin. Oval fibroadenomas often have lobulations. A dark halo around the mass can be seen due to an optical illusion known as the Mach effect caused by an inbuilt edge enhancement mechanism of the human retina.[5] Calcifications can form within an involuting fibroadenoma and are detectable on mammogram, typically in postmenopausal women.[4] Calcification typically starts at the periphery of the mass and coalesces centrally. Fibroadenoma calcifications can range in morphology from round to coarse dystrophic to pleomorphic (**Figure 2B-C**). When beginning to calcify, fibroadenomas may appear suspicious, necessitating further imaging evaluation and biopsy. In a postmenopausal patient, when the calcifications are coarse and "popcorn-like," the diagnosis of involuting fibroadenoma can be made mammographically without further workup. However, a circumscribed mass with calcifications should not be dismissed as an involuting fibroadenoma in a premenopausal woman, as the differential includes cancer.[6] If the morphology of calcifications is suspicious, biopsy may be warranted (**Figure 2D**). Most often, mammographic features of fibroadenoma are nonspecific requiring further evaluation with ultrasound and possibly biopsy depending on sonographic findings.

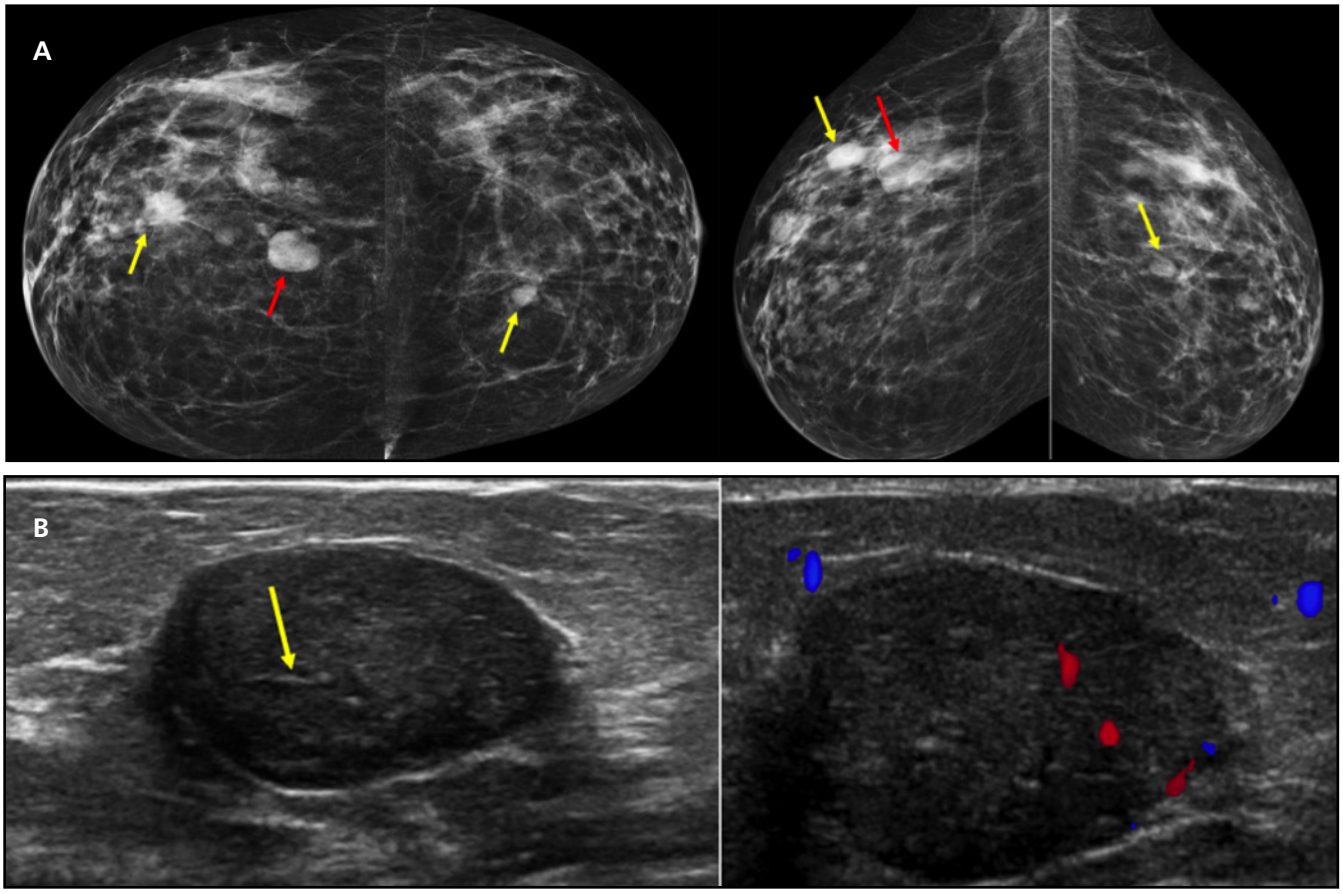


FIGURE 1. *Multiple fibroadenomas. A 32-year-old woman with multiple fibroadenomas in both breasts. (A) Bilateral CC and MLO views show multiple bilateral similar appearing oval, equal density, partially obscured masses in both breasts (yellow and red arrows), with the largest in the right breast at 12:00, 10 cm from the nipple (red arrows). (B) On ultrasound, the dominant mass at 12:00, 10 cm from the nipple shows typical features of fibroadenoma: a hypoechoic, oval, circumscribed, parallel mass with hyperechoic septations (yellow arrow) and posterior acoustic enhancement.*

Contrast-enhanced Digital Mammography (CEDM)

Fibroadenomas may or may not enhance on CEDM. When they do enhance, the level of enhancement is variable. The presence of enhancement may support biopsy, as malignancy typically enhances avidly on CEDM (**Figure 3**). However, the ultimate decision to biopsy must be based on ultrasound morphology.

Ultrasound

On ultrasound, fibroadenomas typically appear as oval, parallel, circumscribed, uniformly hypoechoic masses with echogenic, thin fibrous internal septations (**Figure 1B, 2A**) and variable posterior features. Posterior features depend on mass composition, with more hyalinized masses demonstrating posterior acoustic shadowing and epithelial dominant lesions exhibiting posterior enhancement. Associated calcifications can be seen in approximately 10% and are better characterized on mammography.[1] An echogenic rim, or pseudocapsule, surrounding the mass can be seen secondary to compression of adjacent breast stroma. Internal vascularity is seen in up to 80% on Doppler imaging (**Figure 1B**).[1] When imaging features are not classic (eg, irregular shape or indistinct or microlobulated margins) biopsy should be considered (**Figure 4**).

MRI

Similar to posterior characteristics on ultrasound, the appearance of a fibroadenoma on MRI varies based on the hyalinization of the mass. Hyalinized or sclerotic fibroadenomas appear T2 hypointense. In contrast, cellular or myxoid fibroadenomas are hyperintense on T2 and hypointense on T1-weighted sequences (**Figure 5A-B**). Fibroadenomas show variable enhancement patterns. Myxoid fibroadenomas demonstrate rapid homogeneous contrast enhancement whereas sclerotic fibroadenomas show little to no enhancement. Typical fibroadenomas follow type 1 enhancement kinetics: rapid initial and persistent delayed phases (**Figure 5C**). However, fibroadenomas may have a dynamic contrast enhancement pattern suggestive of malignancy in up to one-third of cases.[7] Classic fibroadenomas will have dark fibrous internal septations (**Figure 5D**). These nonenhancing septations are seen in 40% to 60% of fibroadenomas.[1] While suggestive of fibroadenoma, these septations are nonspecific and other imaging characteristics and clinical factors must be considered.

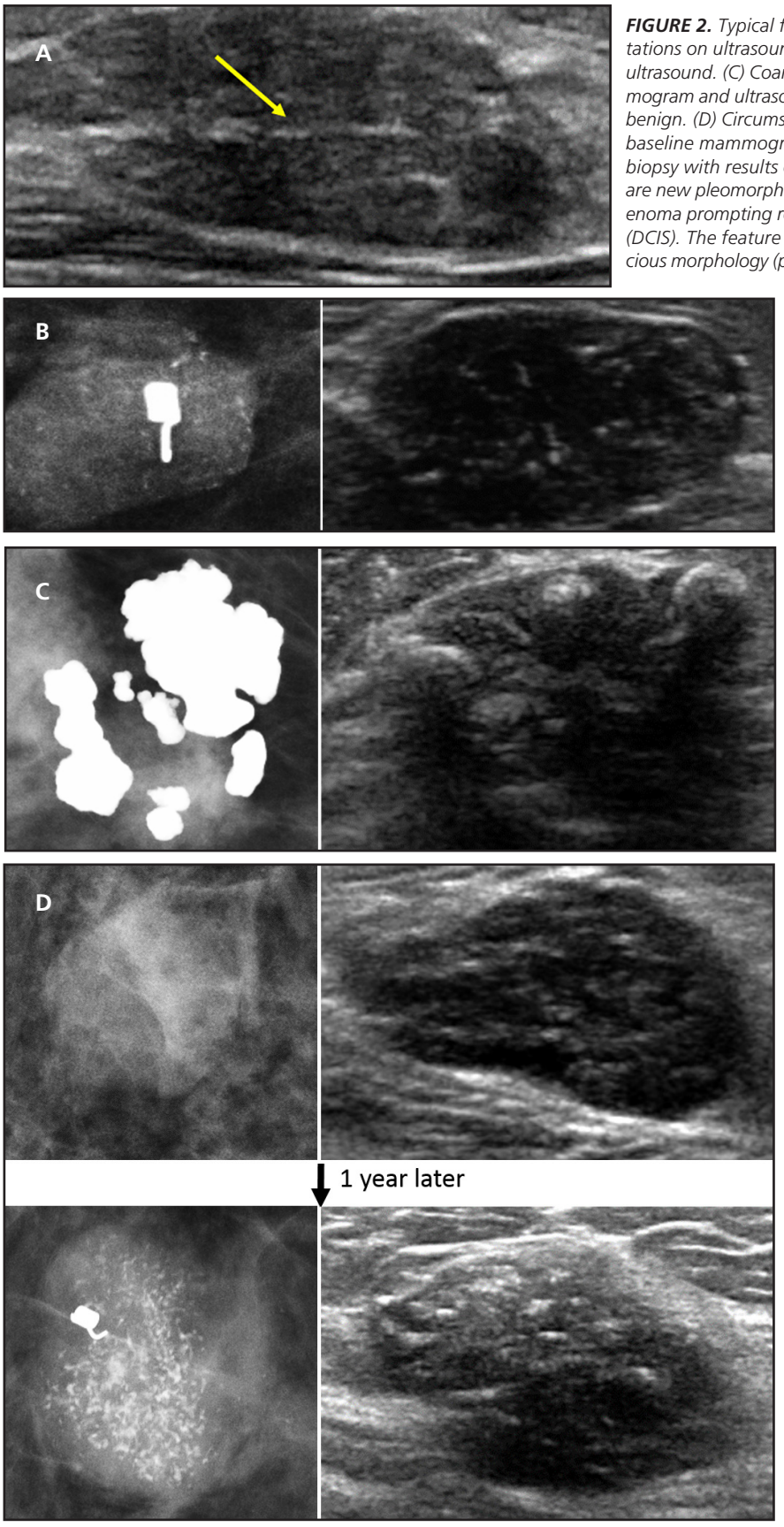


FIGURE 2. *Typical features of fibroadenomas. (A) Hyperechoic septations on ultrasound. (B) Round calcifications on mammogram and ultrasound. (C) Coarse dystrophic ("popcorn") calcifications on mammogram and ultrasound. However, not all calcifications in a mass are benign. (D) Circumscribed oval mass in a premenopausal woman on baseline mammogram and subsequent ultrasound (top) prompted biopsy with results of fibroadenoma. One year later (bottom), there are new pleomorphic calcifications within the biopsy-proven fibroadenoma prompting re-biopsy, which revealed ductal carcinoma in situ (DCIS). The feature warranting biopsy is the presence of new suspicious morphology (pleomorphic) calcifications.*

Differential Considerations and Atypical Imaging Presentations

Variants of fibroadenoma are important to consider, as their management differs slightly from typical fibroadenomas. A juvenile fibroadenoma is a variant seen primarily in adolescence. Apart from patient age, larger size, and characteristic rapid growth (**Figure 6**), these masses cannot be distinguished from typical fibroadenomas by imaging. At pathology, they are differentiated by the increased stromal hypercellularity of juvenile fibroadenomas.[1] In contrast to typical fibroadenomas, they are usually treated with excision given the rapid growth and larger size.

Another variant is a complex fibroadenoma. While these cannot be completely distinguished from fibroadenoma on imaging, sonographic features suggestive of a complex fibroadenoma include internal heterogeneity, cysts, and punctate echogenic foci. Awareness of these features is important because their presence may motivate biopsy in lieu of routine follow-up. Upon biopsy, complex fibroadenomas may demonstrate cysts, sclerosing adenosis, epithelial calcifications, or papillary apocrine changes.[1] Diagnosis of a complex fibroadenoma has been associated with an increased risk of invasive breast cancer for both breasts. Dupont et al showed that the relative risk of invasive breast cancer is 3.10 times higher for women with complex fibroadenomas compared to 2.17 times higher for patients with typical fibroadenomas.[8] However, a recent study performed by Nassar et al found that complex fibroadenomas do not confer increased risk of breast cancer

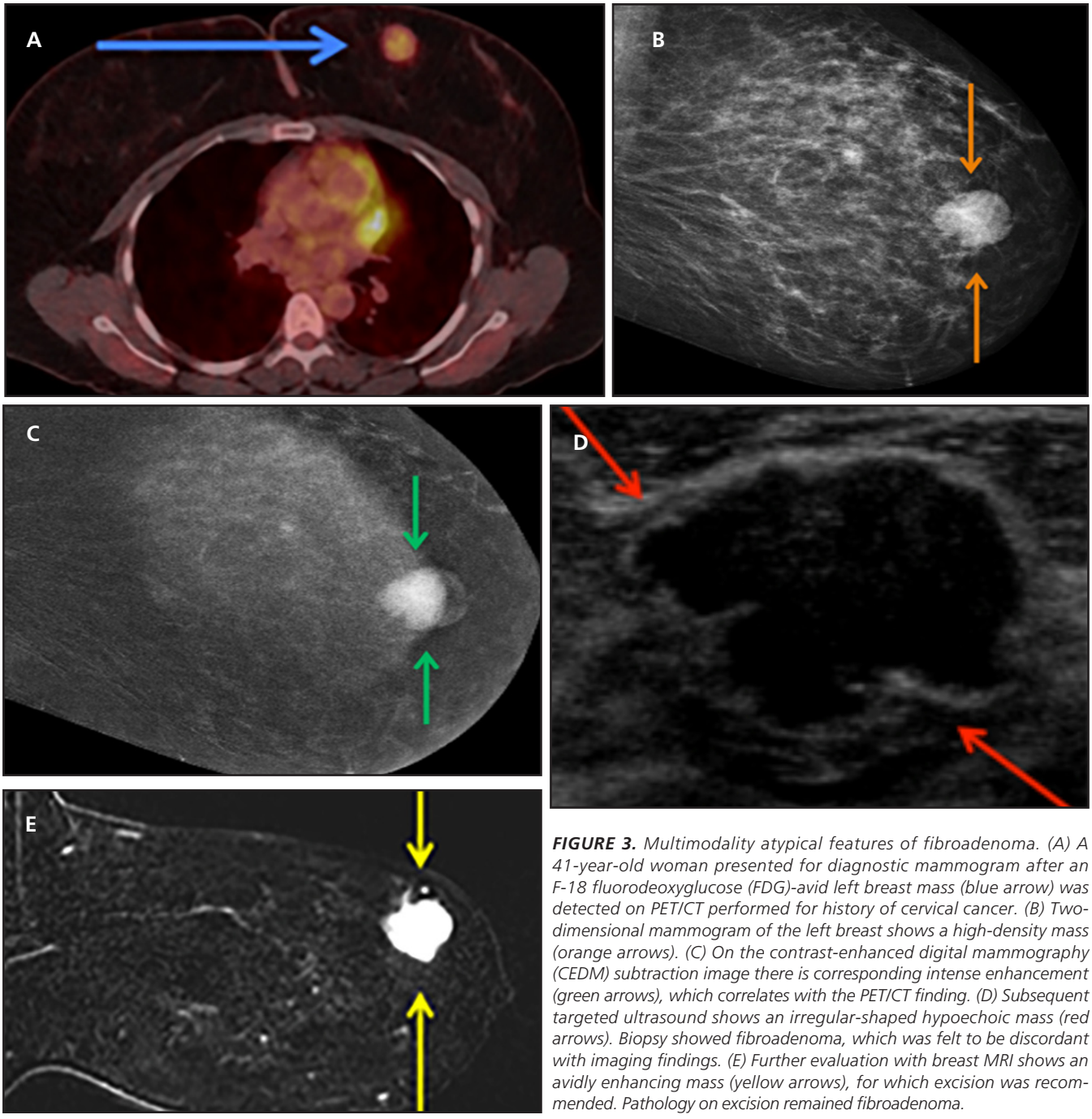


FIGURE 3. *Multimodality atypical features of fibroadenoma. (A) A 41-year-old woman presented for diagnostic mammogram after an F-18 fluorodeoxyglucose (FDG)-avid left breast mass (blue arrow) was detected on PET/CT performed for history of cervical cancer. (B) Two-dimensional mammogram of the left breast shows a high-density mass (orange arrows). (C) On the contrast-enhanced digital mammography (CEDM) subtraction image there is corresponding intense enhancement (green arrows), which correlates with the PET/CT finding. (D) Subsequent targeted ultrasound shows an irregular-shaped hypoechoic mass (red arrows). Biopsy showed fibroadenoma, which was felt to be discordant with imaging findings. (E) Further evaluation with breast MRI shows an avidly enhancing mass (yellow arrows), for which excision was recommended. Pathology on excision remained fibroadenoma.*

beyond that of the established histologic features and should be managed based on the associated histologic findings.[9]

Another key differentiation is that between fibroadenoma and phyllodes tumor, another fibroepithelial lesion of the breast. In contrast to fibroadenomas, phyllodes tumors, although rare, may have locally aggressive or frankly malignant potential and should be managed surgically.[10] Thus, the differentiation between the two is clinically significant. Fibroadenoma and phyllodes tumor share many common imaging findings and it is difficult to distinguish them on all breast imaging modalities (**Figure 7A**). The presence of intralesional clefts and cystic spaces on ultrasound may favor phyllodes tumor (**Figure 7B**).[11] However, these features have not been found reliably useful for differentiation. A study on MRI differentiation of these lesions found a nonsignificant difference in heterogeneous inner structure and nonenhancing septation, with phyllodes tumors displaying these features more often than biopsy-proven fibroadenomas.[7] In spite of these subtle differences, ultimately the study found that phyllodes tumors and fibroadenomas cannot be precisely differentiated on breast MRI. Diagnosis is further complicated by similar clinical presentation; however,

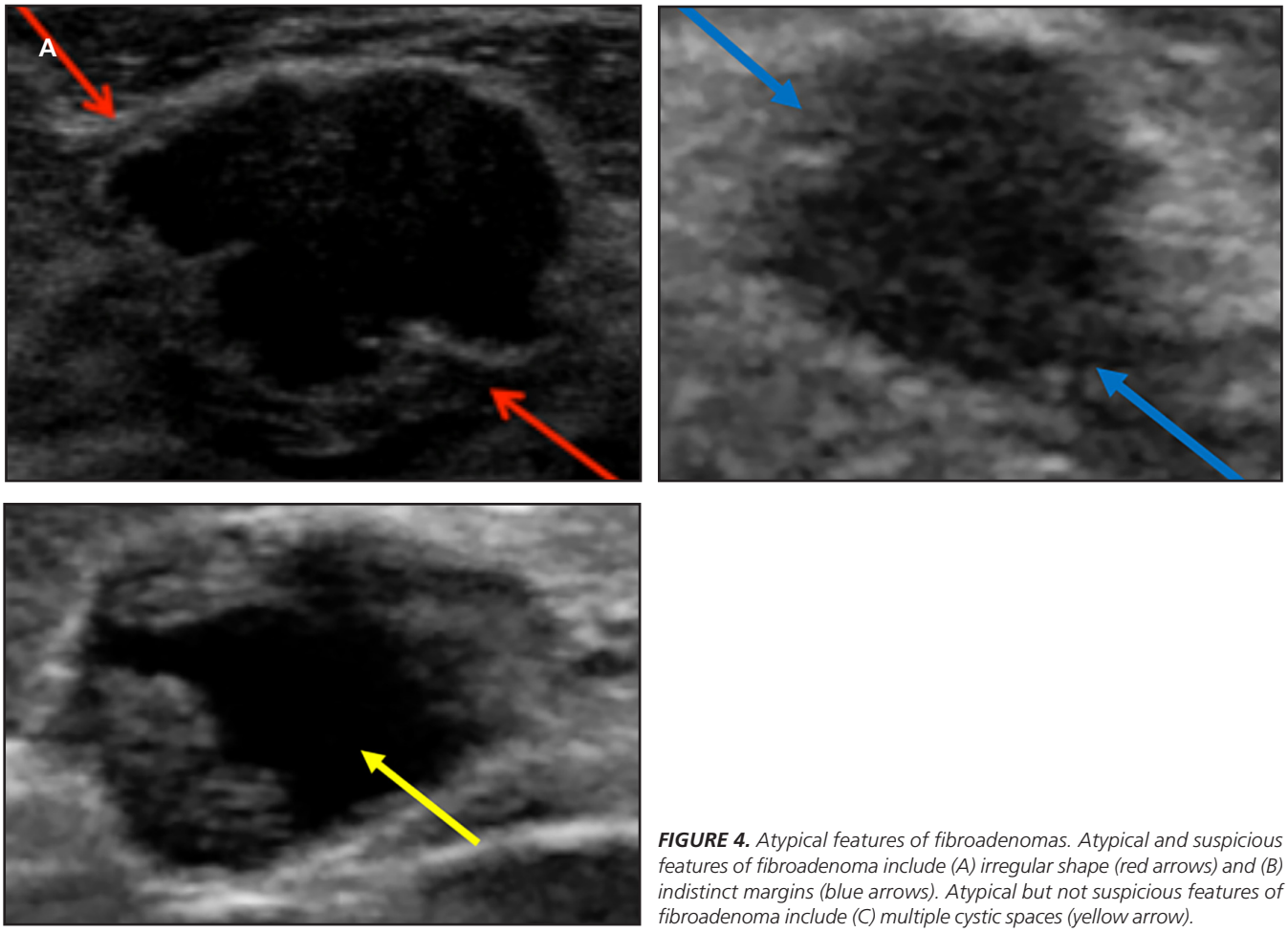


FIGURE 4. *Atypical features of fibroadenomas. Atypical and suspicious features of fibroadenoma include (A) irregular shape (red arrows) and (B) indistinct margins (blue arrows). Atypical but not suspicious features of fibroadenoma include (C) multiple cystic spaces (yellow arrow).*

phyllodes tumors tend to be diagnosed later in life compared with fibroadenomas, with a median age at presentation of 42 to 45 years.[12,13]

In addition to phyllodes tumors, imaging features of fibroadenoma also overlap with other fibroepithelial lesions including tubular adenoma and lactational adenoma. Tubular adenomas are rare and found primarily in younger women. Tubular adenomas can have varied appearance related to the patient's age. In younger patients, they appear as a noncalcified, circumscribed, solid mass, similar to a fibroadenoma (**Figure 8**). In older patients, they can appear as suspicious, irregular masses with microcalcifications requiring core biopsy, although this is less common.[14]

Lactational adenomas are a common solid breast mass diagnosed during pregnancy thought to arise due to the physiologic changes of pregnancy and lactation. Some regard this mass as a variant of fibroadenoma, tubular adenoma, or lobular hyperplasia that has undergone histologic changes as a result of the physiologic state induced by pregnancy (**Figure 9**).[3] They appear on ultrasound as oval, circumscribed, homogeneous, hypoechoic to isoechoic masses, indistinguishable from fibroadenomas. They may have hyperechoic areas, representing inspissated milk, and posterior enhancement secondary to the fluid component, which can serve as useful diagnostic signs on ultrasound.[1,3] On mammogram, they can have radiolucent areas representing the fat content of the milk secondary to lactational hyperplasia. Rarely, lactational adenomas can appear suspicious on ultrasound with irregular contours and posterior acoustic shadowing.[3] Lactational adenomas require tissue sampling or close surveillance with tissue sampling favored when imaging is atypical; although, there is a small risk for milk fistula after core biopsy.

While it is difficult to distinguish between the different benign fibroepithelial lesions on imaging, it can also be challenging to distinguish between fibroadenomas and malignant masses. Ultrasound features of BRCA-associated breast cancers can resemble a benign mass, such as a fibroadenoma. BRCA-associated breast cancer can appear as a round, circumscribed, hypoechoic and homogenous mass with increased through transmission (**Figure 10A-B**).[15] Knowing the patient's personal and family history and BRCA status, if tested, is crucial in determining management of a mass on mammogram, ultrasound, or MRI. What may look like a classic fibroadenoma in an average-risk patient may be a breast cancer in a BRCA-positive or

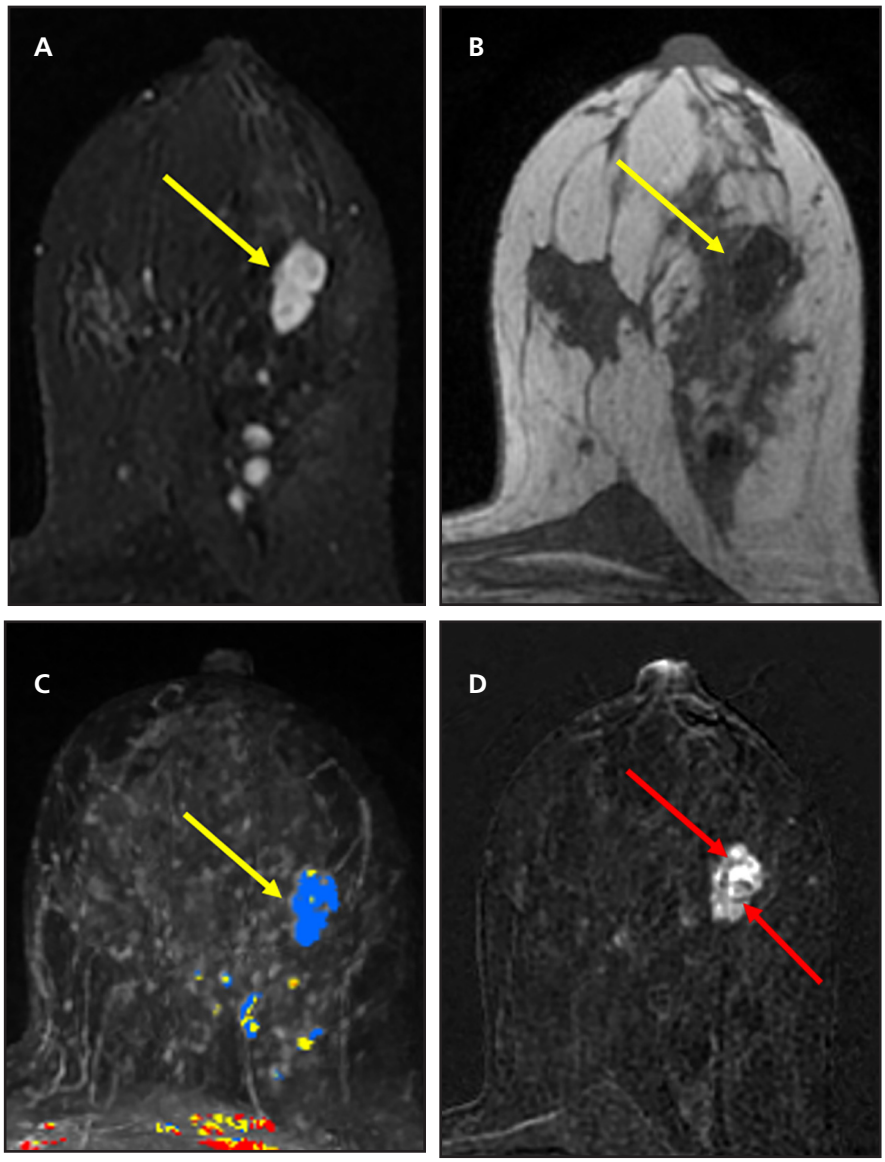


FIGURE 5. *Fibroadenoma on MRI. A 53-year-old woman with multicentric right breast cancer presented for evaluation with breast MRI after adjuvant chemotherapy. In the contralateral left breast is a 1.7 x 1.0 cm mass (yellow arrows) at the 3:00 position, 4 cm from the nipple. The mass is (A) T2 hyperintense, (B) T1 hypointense with (C) persistent kinetics and (D) nonenhancing septations (red arrows) on subtraction image, consistent with and corresponding to a previously biopsied fibroadenoma.*

other high-risk patient (**Figure 10C-F**). Thus, biopsy rather than periodic imaging follow-up is more readily performed for benign or probably benign masses in high-risk patients due to their increased lifetime risk of developing breast cancer.

MRI, one of the key screening modalities in the BRCA-positive population owing to its sensitivity, cannot reliably distinguish benign entities from malignancy. For example, fibroadenomas may have a dynamic contrast-enhancement pattern suggestive of malignancy in up to one-third of cases.[7] Additionally, mucinous carcinoma, which is typically T2 hyperintense, often mimics a probably benign lesion.[7] High-grade cancers may have circumscribed margins, a typically benign feature, due to fast cellular growth rates allowing minimal time for the reactive parenchymal changes that contribute to the appearance of a morphologically malignant, spiculated mass.

Breast-specific gamma imaging (BSGI) and its predecessor scintimammography are other modalities used primarily as adjunctive screening tools in high-risk women. When used with mammography for breast cancer screening in women at increased risk and with dense breasts, BSGI significantly improves sensitivity and positive predictive value. BSGI also increases the number of breast cancers detected, as it has been shown to detect mammographically occult breast cancer.[16] BSGI uses the radiotracer Tc-99m sestamibi to identify physiological differences between malignant and normal breast tissue.[16] Focally increased radiotracer uptake is the hallmark of malignancy on BSGI (**Figure 11**). However, fibroadenomas can present a diagnostic quandary. While generally "cold" on BSGI (**Figure 12**), fibroadenomas and other benign breast disease can appear "hot", with increased radiotracer uptake relative to background (**Figure 13**), similar to other functional modalities, such as MRI and CEDM. In fact, fibroadenomas, fibrocystic disease and inflammatory lesions are regarded as well-known causes of false-positive Tc-99m sestamibi uptake. In these cases, dual-phase imaging in BSGI may help discriminate between benign and malignant lesions based on the assumption that Tc-99m sestamibi uptake by cancerous cells might persist on delayed images compared with benign conditions.[17] A recent study showed that in 11 false positive cases, 9 patients showed tracer washout one hour after tracer injection, supporting this notion.[17]

Treatment Options for Fibroadenoma

If classic features of fibroadenoma are present, the lesion can be followed by imaging every 6 months for 2 years (or at 6, 12 and 24 months) without core biopsy. There is a growing body of evidence showing that periodic imaging surveillance is a safe management option for probable fibroadenomas. A study about long-term follow-up performed

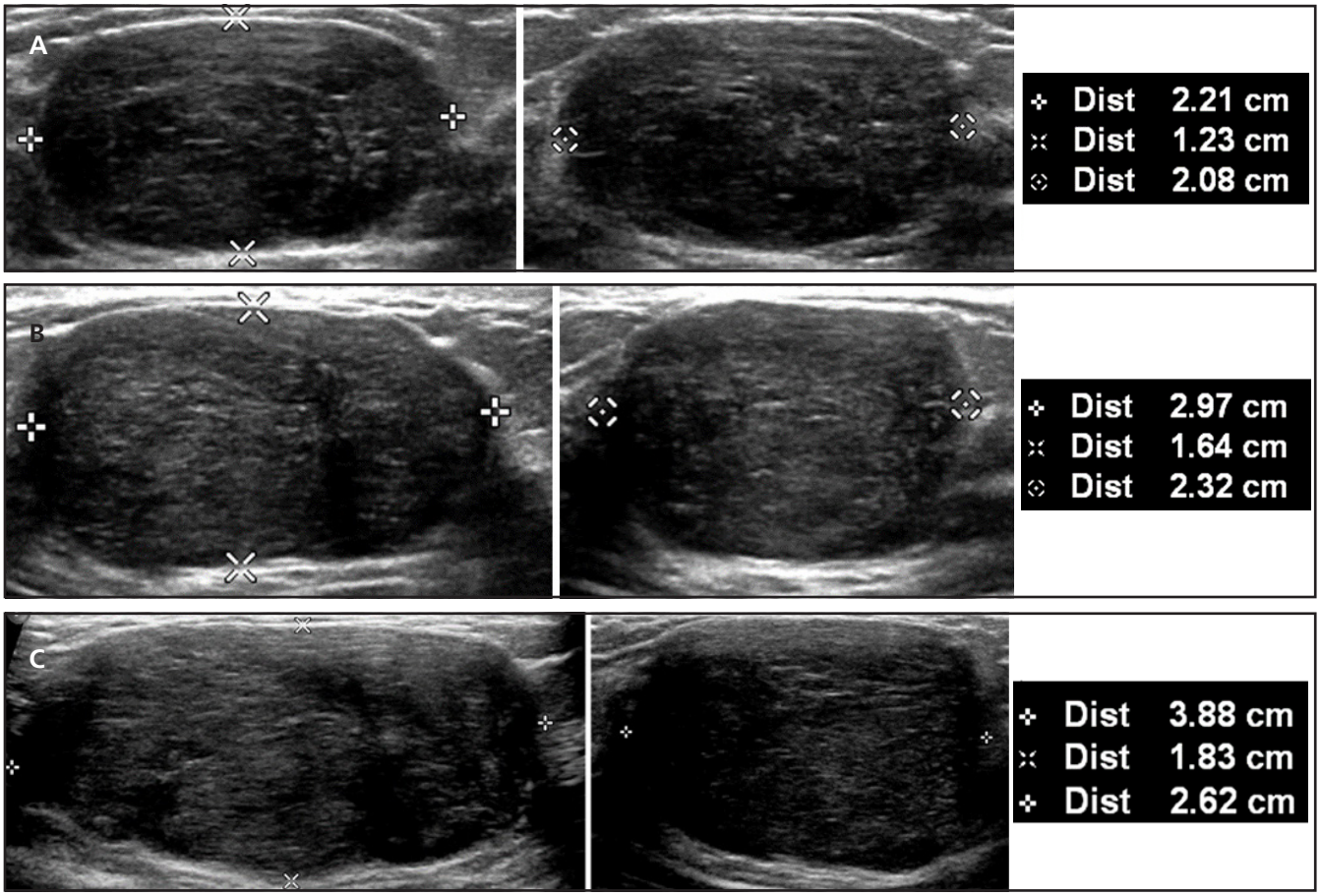


FIGURE 6. *Juvenile fibroadenoma. An 18-year-old woman presented with a palpable lump in the left breast. (A) Ultrasound in the area of palpable concern shows a 2.2 x 1.2 x 2.1 cm oval, hypoechoic parallel mass with circumscribed margins, categorized as BIRADS 3. (B) On follow-up imaging 6 months later, the mass has enlarged to 3.0 x 1.6 x 2.3 cm. Biopsy at that time showed fibroadenoma and was categorized as BIRADS 2. (C) Six months after the biopsy, the patient returned with concerns for further enlargement of the previously biopsied left breast mass. (C) Ultrasound shows the previously documented mass has enlarged to 3.9 x 1.8 x 2.6 cm. Surgical excision was performed due to significant growth with final pathology of juvenile fibroadenoma.*

by Gordon et al reported that fibroadenomas may be safely followed with volume growth rates of up to 16% per month for patients < 50 years old and up to 13% per month in those ≥ 50.[18] This study determined that the acceptable mean change in size for all ages was equivalent to a 20% increase in all 3 dimensions in a 6-month period.[18] If > 20% growth is observed during the follow-up period, biopsy should be performed.

Choosing to biopsy a probable fibroadenoma is practice and patient specific. The patient's personal history, family history, and age are taken into account in conjunction with imaging features of the mass when deciding to biopsy. If any imaging features other than the classic features are present, or if the clinical presentation raises a concern for malignancy or a phyllodes tumor (rapid growth, new presentation after menopause, etc.), a biopsy is recommended. Fibroadenomas with epithelial abnormalities found at core biopsy require surgical excision, even though occurrence of malignancy in or adjacent to a biopsy-proven fibroadenoma is rare.[19] Fibroadenomas without epithelial abnormality diagnosed by core biopsy need no specific follow-up and can be left alone if asymptomatic. For symptomatic patients wanting definitive treatment for a fibroadenoma, options include surgical excision or minimally invasive techniques, such as ablative procedures and vacuum-assisted core biopsy. Generally, women with fibroadenomas measuring > 3 cm are sent for surgical consultation.

Surgical Excision

Surgical excision is the most utilized strategy for definitive treatment of a fibroadenoma. Approximately 500,000 fibroadenomas are treated by surgical excision each year.[20] Surgery is the best option for a symptomatic woman and a consult should be considered**.** Giant fibroadenomas, also known as juvenile fibroadenomas, require surgical excision due to associated complications including breast distortion, potential for psychological harm, and rapid enlargement that may cause venous congestion, glandular distortion, pressure necrosis and ulceration.[20] While surgery

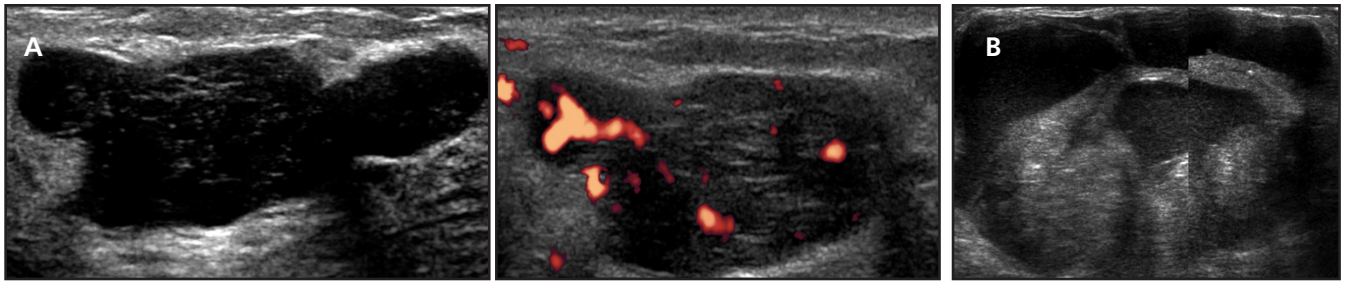


FIGURE 7. *Phyllodes tumor. (A) A 30-year-old woman presented with a palpable lump in the right breast, present for 8 years, with new enlargement and pain. Gray-scale (left) and color Doppler (right) sonography was performed on the area of concern. At the 12:30 position in the right breast there is a 3.3 x 1.2 x 1.9 cm oval mass with a few lobulations, posterior acoustic enhancement and internal vascularity. Subsequent biopsy revealed a fibroepithelial lesion with cellular stroma consistent with cellular fibroadenoma. Surgical excision was performed due to presence of cellular stroma with final pathology of Phyllodes tumor. (B) A 45-year-old woman presented for a left breast mass that had been growing over the last 2 years. Gray-scale ultrasound image shows a large 8.2 x 5.5 x 7.0 cm, complex cystic and solid mass. Internal vascular flow was demonstrated with color Doppler (not pictured). Biopsy and subsequent excision revealed Phyllodes tumor.*

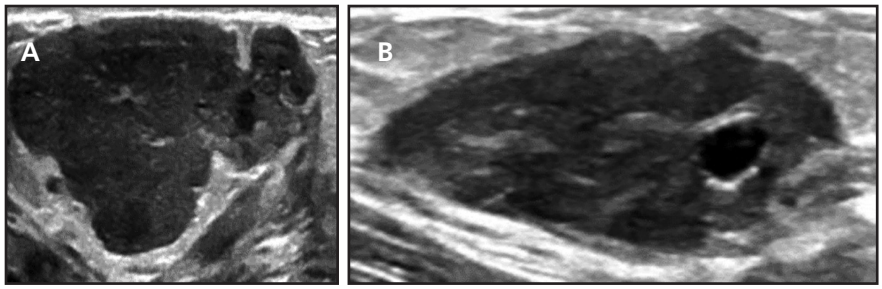


FIGURE 8. *Tubular adenoma. A 29-year-old woman presented with 2 palpable masses in the left breast. On gray-scale sonography, 2 left breast masses are seen at (A) 3:00 and the (B) 12:30 position. Both masses have heterogeneous hypoechogenicity and small anechoic internal cystic spaces. Both were biopsied with results of tubular adenoma.*

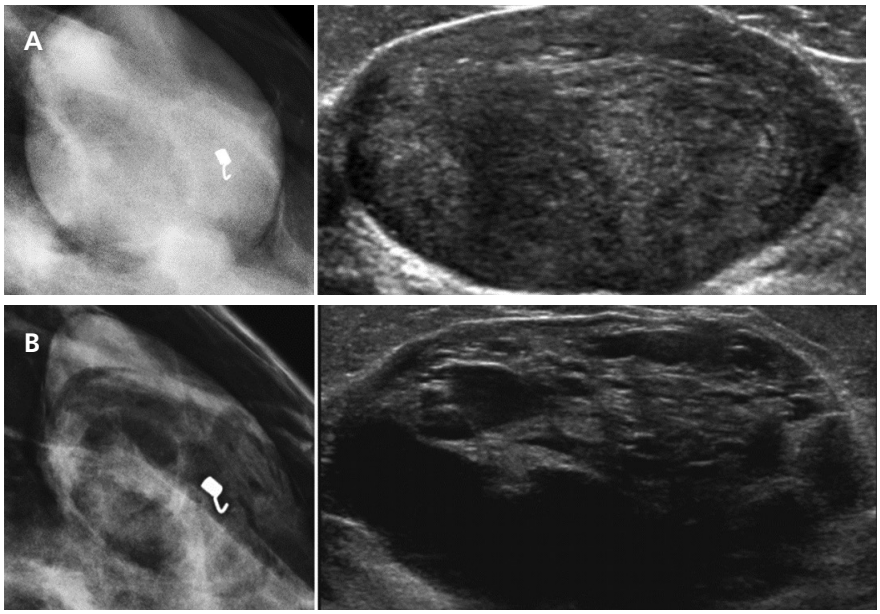


FIGURE 9. *Fibroadenoma with lactational change. (A) A 40-year-old woman has a history of biopsy-proven fibroadenoma seen as a circumscribed, oval, equal-density mass on mammogram (left) and as a 3.0 x 1.7 x 2.9 cm oval, circumscribed, hypoechoic left breast mass at 2:00, 5 cm from the nipple on ultrasound (right). The same woman presented at 4 months postpartum with concerns that the known left breast mass was enlarging. (B) Mammogram (left) shows a circumscribed oval mass with low density and equal density components within the biopsy-proven fibroadenoma. Ultrasound (right) of the area of palpable concern shows a 4.6 x 2.1 x 3.7 cm circumscribed, oval, parallel, complex cystic and solid mass compatible with lactational change in the existing fibroadenoma.*

allows for complete resection, there are risks associated with general anesthesia as well as a greater potential for poor cosmetic outcomes requiring an additional reconstructive surgery. Given the nonmalignant nature of fibroadenomas, an important treatment goal should be cosmesis. A study by Cochrane et al found that the best cosmetic outcomes and highest patient satisfaction occurred when < 10% of the breast volume was excised.[21] Minimally invasive surgical techniques, such as endoscopic lumpectomy, have been pursued for improved cosmesis. In this procedure, 3 small incisions are made in the midaxillary line, a trocar is inserted in the region of the tumor, and carbon dioxide gas is insufflated into the chest wall to facilitate tumor access. The tumor is then dissected and retrieved, either intact or piecemeal depending on initial size, with a specimen retrieval bag.[20] Endoscopic removal by this extramammary approach has been proposed as the best option for benign breast tumors, such as fibroadenomas, considering the young age of the patient population and the excellent cosmetic outcomes.[22] Nevertheless, open excision is still more common. Effort is also made to improve cosmesis in open breast-conserving surgery by making incisions in the circumareolar region or the inframammary crease.[20]

Minimally Invasive Techniques

In addition to minimally invasive surgical approaches, minimally invasive office-based procedures have been

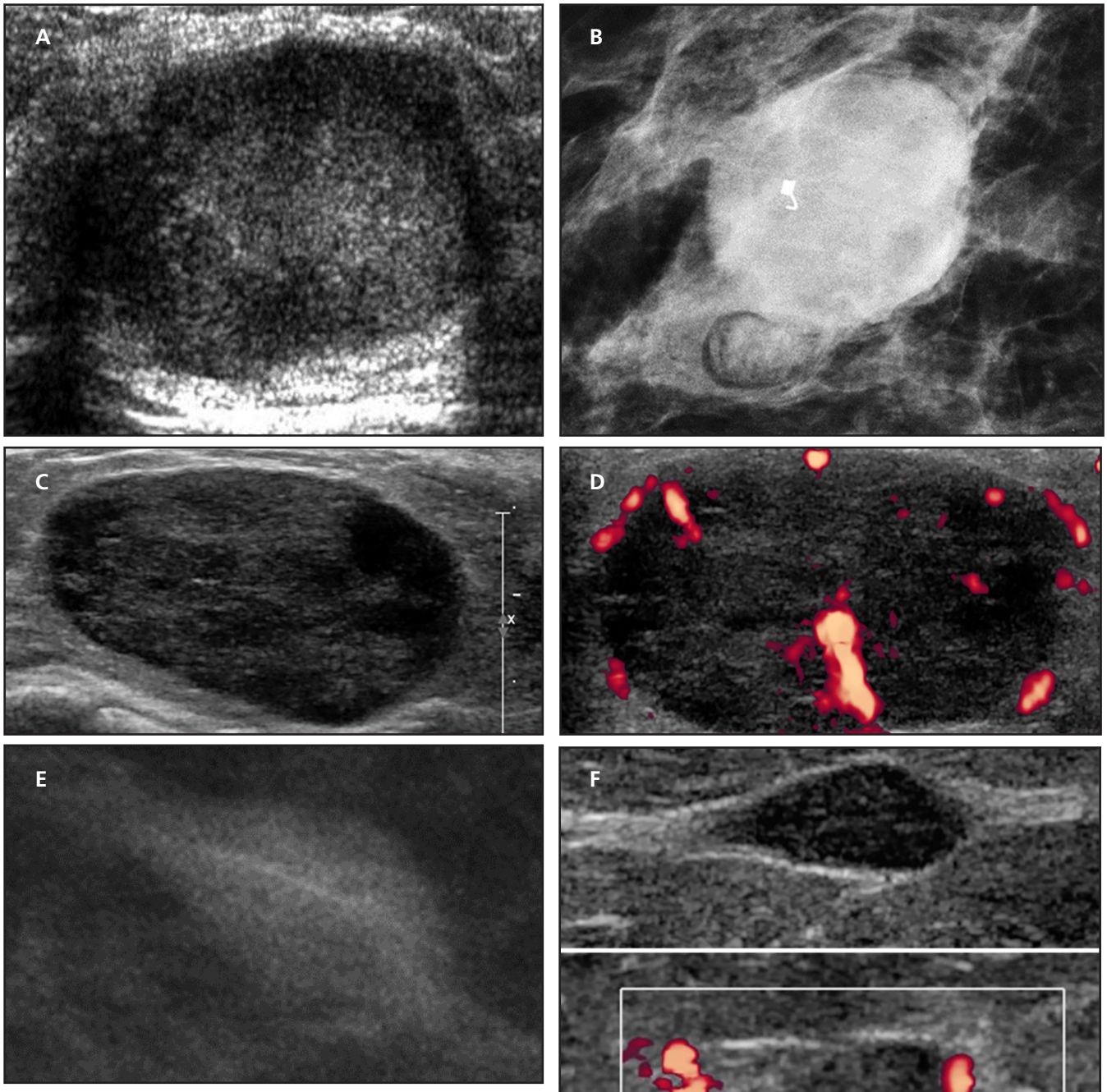


FIGURE 10. *Cancer mimicking fibroadenoma. (A,B) A 57-year-old woman with known BRCA gene mutation presented for a palpable right breast mass. (A) Initial ultrasound shows a hypoechoic, parallel mass with circumscribed margins and posterior acoustic enhancement. Subsequent biopsy was performed. (B) Postbiopsy mammogram shows a hyperdense, oval, circumscribed mass containing a coil-shaped biopsy clip. Biopsy results were invasive ductal carcinoma. The patient went on to have a modified radical mastectomy. As seen in this case, BRCA-associated cancers may exhibit benign features, and more liberal biopsy thresholds should be utilized in high-risk patients. (C,D) A 75-year-old woman with a personal history of left breast invasive ductal carcinoma treated with left mastectomy presented with a left chest wall mass. (C) Gray-scale and (D) color Doppler sonography was performed on the area of palpable concern showing a mass, which appears indistinguishable from a benign fibroadenoma on imaging alone. However, given the patient history, this mass is suspicious. Biopsy was performed revealing invasive ductal carcinoma. (E,F) A 66-year-old woman with a remote personal history of right breast cancer treated with breast conservation therapy presented for an annual screening mammogram. (E) The mammogram shows an oval, partially obscured right breast mass. (F) Gray-scale (top) and power Doppler (bottom) images from targeted ultrasound show a solid, oval, circumscribed, homogeneous, hypoechoic mass. The mass was biopsied with results of papillary carcinoma.*

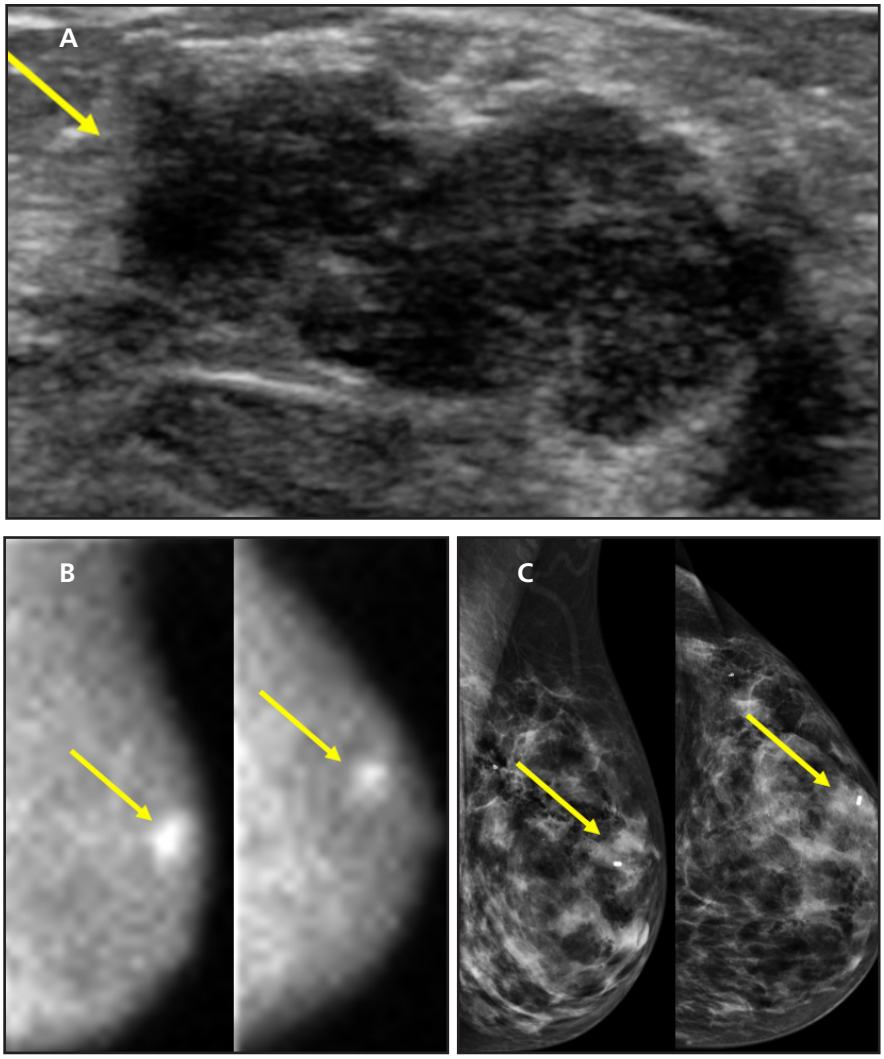


FIGURE 11. *Cancer mimicking fibraodenoma with breast-specific gamma imaging (BSGI) correlation. A 34-year-old woman with a family history of breast cancer in her mother and grandmother presented for a palpable left breast lump. (A) Ultrasound shows a microlobulated, hypoechoic mass with irregular margins at the 1:00 position (yellow arrow). (B) A subsequent BSGI study shows increased isotope uptake correlating to the 1:00 position palpable mass (yellow arrows). Subsequent biopsy revealed fibroadenoma. (C) Postultrasound-guided biopsy mammogram shows a biopsy clip in the region of increased isotope uptake (yellow arrows). Biopsy results were considered discordant based on ultrasound and BSGI imaging findings. The patient went on to have an excisional biopsy with results of invasive ductal carcinoma.*

used in treating fibroadenoma. Office-based techniques performed under local anesthesia lack the risks of general anesthesia and are relatively painless compared to open surgery. They also promise improved cosmetic outcomes, with little to no tissue loss during percutaneous ablative techniques. Office-based procedures are also more cost effective. Surgical techniques, however, have the advantage of allowing for additional pathologic analysis upon removal.

Vacuum-Assisted Breast Biopsy— Small (< 2 to 3 cm) fibroadenomas can be removed under image guidance using a vacuum-assisted device, similar to that used for vacuum-assisted core needle biopsy. Multiple samples are obtained with the needle until the mass appears completely removed. Complete excision is not guaranteed and hemorrhage and hematoma can result due to the multiple samples required for removal, especially when fibroadenomas are > 2 cm. Hematoma formation occurs at a rate of 0% to 13%.[20] Removal of the lesion ranges from 22% to 98% depending on the quality of imaging technique, needle gauge, and initial size of the lesion.[20] This technique is not utilized for malignant lesions due to the risk of incomplete removal. Despite incomplete removal and resulting risk of recurrence, patients report high satisfaction with the procedure and prefer it to surgical excision.[2] The American Society of Breast Surgeons (ASBrS) endorses ultrasound-guided percutaneous excision of fibroadenomas in their 2008 statement as a safe, effective and well-tolerated procedure with minimal cost, low morbidity, and desirable cosmetic outcomes.

Percutaneous Ultrasound-Guided Cryoablation— Percutaneous cryoablation is an FDA-approved non-surgical option for patients desiring definitive, minimally invasive treatment of a fibroadenoma. Cryoablation is also endorsed by the ASBrS in their 2008 statement as a safe and efficacious treatment for fibroadenoma. Careful patient selection is made using ASBrS criteria for cryoablation of fibroadenoma including the need for visibility by ultrasound, definitive histologic confirmation with core biopsy, and size < 4 cm. Although it is a well-accepted treatment option in the medical community, cryoablation is not widely utilized as many insurance companies categorize it as investigational.

Cryoablation systems use a cooling gas under pressure inside a shielded probe to freeze adjacent tissue. Real gases change temperature relative to pressure when forced through a valve and heat exchange with the environment is prevented. This principle is known as the Joule-Thomson Effect, or throttling process, and is the basis of cryoablation systems. The amount and direction of temperature change depends on the Joule-Thomson coefficient of a gas, which represents the

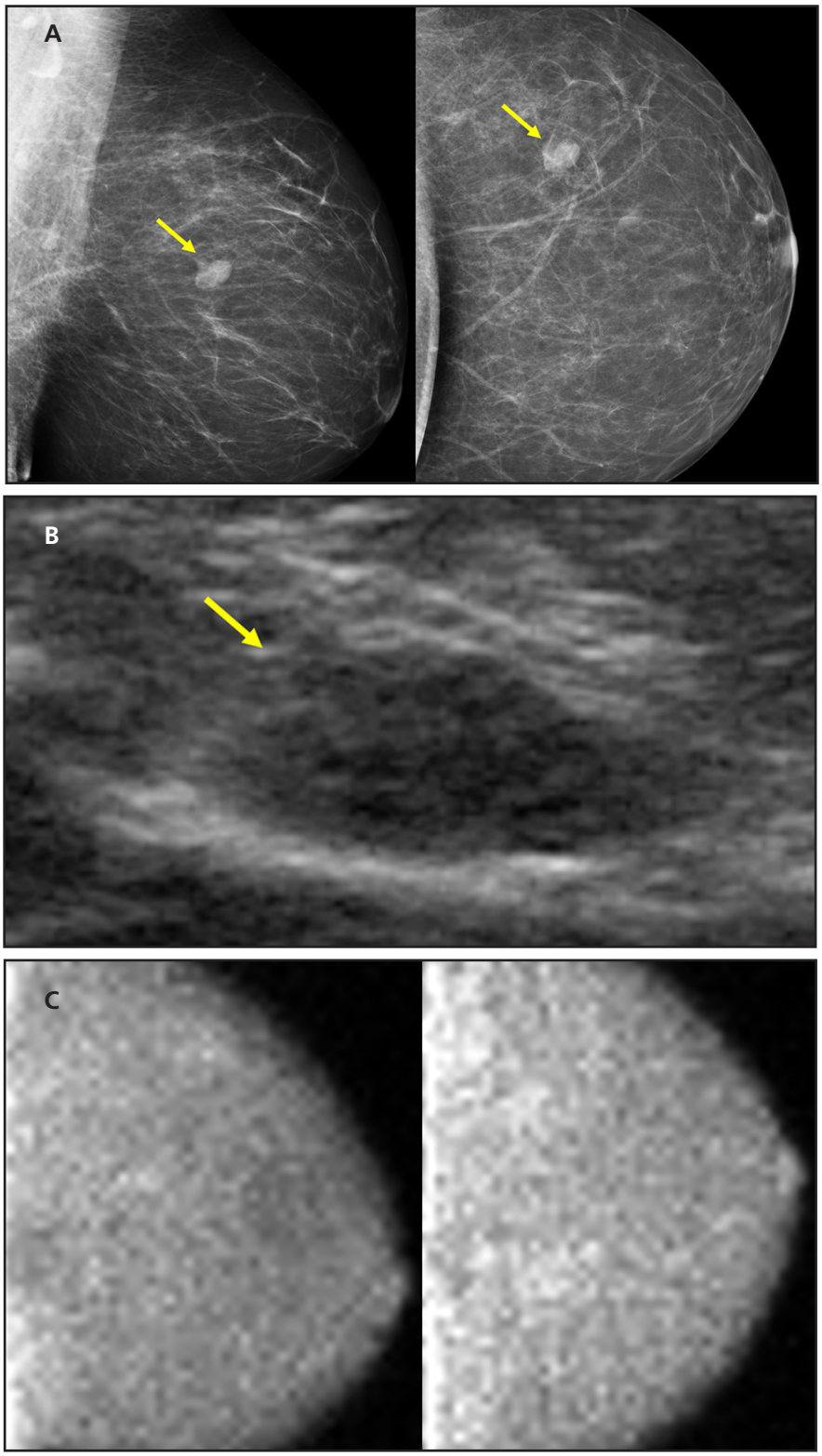


FIGURE 12. *Typical fibroadenoma features on breast-specific gamma imaging (BSGI). (A) A 39-year-old woman presented for a screening mammogram, which shows a 1.6 cm oval, circumscribed mass at the 3:00 position (yellow arrow). (B) On subsequent diagnostic ultrasound, this correlates with a 1.6 cm oval, hypoechoic mass with circumscribed margins. (C) Subsequent BSGI study shows no abnormal isotope uptake, supporting the mammographic and sonographic features of a fibroadenoma, which was categorized as a BIRADS 2.*

rate of temperature change relative to pressure. Nitrogen or argon gas is used most commonly in cryoablation systems based on their favorable coefficients.

During the procedure, a 9- or 10-gauge cryoablation probe is inserted into the center of the breast tumor under real-time sonographic guidance after administration of local anesthesia. High-pressure gas is forced through the center chamber of the dual-chambered probe. At the tip of the probe, the gas enters the expansion chamber where pressure decreases and the gas cools. The cold gas absorbs heat energy from the surrounding tissue via conduction, lowering tissue temperature and freezing the adjacent tissue, creating an "ice ball" (**Figure 14**). Tissue temperature is coldest adjacent to the probe, reaching -140°C to -160°C, and increases as distance from the probe increases. The visible rim of the ice ball represents the 0°C isotherm, which is not tissue lethal. The lethal isotherm is not visible. It is typically located at least 5 mm central to the outer edge, with lethal temperatures -20°C to -40°C depending on tissue type.[23] For effective treatment, the lethal zone must cover the entire target lesion with at least a 5-mm ablation margin. The diameter of the "ice ball" is determined by the flow of gas and the length of the "ice ball" is determined by uninsulated probe length. If necessary, multiple probes can be utilized to increase the lethal zone. Precaution must be taken to ensure that the "ice ball" does not extend to involve other structures. One trial for cryoablation of breast cancer required that the mass was > 5 mm deep to the skin and nipple.[24] However, in practice, there is no official criteria defining an acceptable distance from other structures. Techniques, such as injecting saline to create a buffer between the mass/treatment area and skin, can help prevent unintended damage.

The cryoablation procedure consists of a freeze-thaw-freeze cycle and

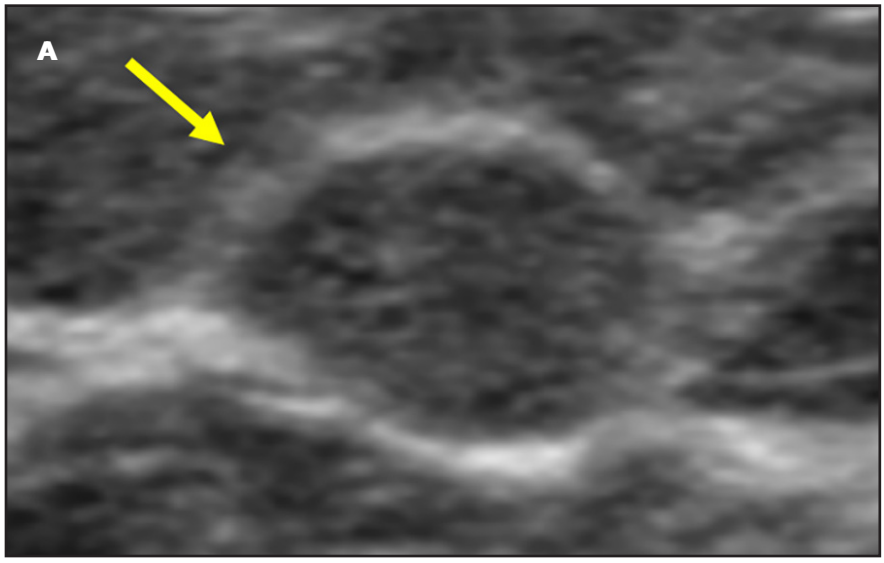
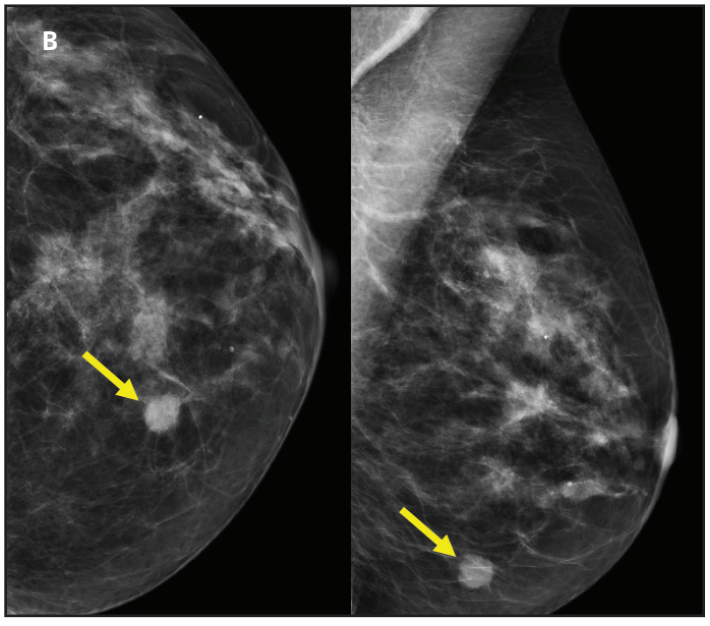
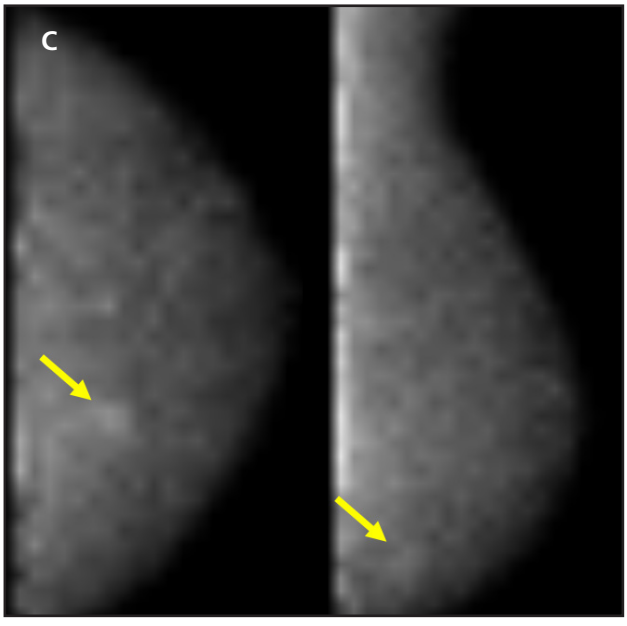


FIGURE 13. *False positive fibroadenoma on breast-specific gamma imaging (BSGI). A 51-year-old woman with (A) a 0.7 x 0.7 x 0.5 cm hypoechoic, oval, circumscribed mass in the left breast seen on ultrasound was further evaluated. (B) Mammogram shows a hyperdense round mass in the lower inner left breast correlating to the sonographic mass. (C) Subsequent BSGI study performed for a contralateral breast finding shows mild increased uptake within the mammographically stable mass, presumed to represent fibroadenoma.*





can take up to 25 minutes depending on tumor size. This cycle destroys tumor cells through direct cell damage and death, vascular injury and ischemia, and indirect immunologic mechanisms.[25] During freezing, there is formation of intracellular, extracellular, and intravascular ice. Intracellular ice causes pore formation in the cell wall. Extracellular ice decreases extracellular free water and increases extracellular osmolarity. As a result, water exits the intracellular compartment causing cell shrinkage and dehydration.

During thawing, extracellular ice melts before intracellular ice causing increased free extracellular water. Endothelial damage caused by intravascular ice increases vascular permeability and contributes to increased extracellular water and decreased extracellular osmolarity. Osmotic gradients force water inside cells during thawing, causing cells to swell and burst leading to cell damage and death.[25] Delayed immune response then leads to absorption of damaged tissue, taking up to one year for the fibroadenoma and treatment zone to become nonpalpable. There is no routine follow-up imaging required for patients after cryoablation of fibroadenoma. Patients are followed clinically with a focus on palpability of the fibroadenoma and treatment zone.

Multiple studies have assessed outcomes of cryoablation for fibroadenomas. For example, Littrup et al found that 89% of all fibroadenomas, independent of original size were nonpalpable at 12 months.[26] Kaufman et al in 2004 found that 75% of all fibroadenomas were nonpalpable at one year with a 92% patient satisfaction rate.[27] In 2005, Kaufman et al demonstrated that 84% of previously palpable fibroadenomas and 94% of fibroadenomas ≤ 2 cm were nonpalpable at an average follow-up time of 2.6 years with a 97% patient satisfaction rate.[28] They also showed a 99% median volume reduction of treatment zone by ultrasound in that

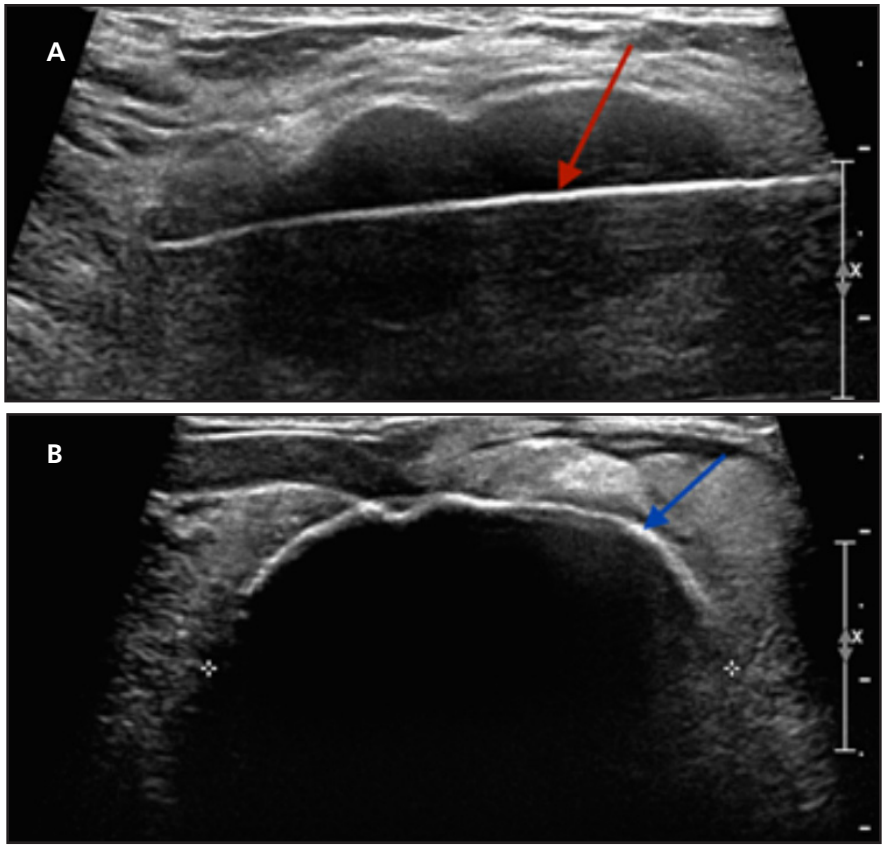


FIGURE 14. *Fibroadenoma cryoablation. Percutaneous ultrasound-guided cryoablation was performed for a biopsy-proven fibroadenoma < 4 cm and visible by ultrasound. (A) A sonographic image taken during the procedure shows the cryoablation probe (red arrow) centered in the fibroadenoma. (B) A subsequent intraprocedural image shows the "ice ball" formed after the freeze-thaw-freeze cycle (blue arrow indicates the edge of the ice ball, the 0 °C isotherm).*

follow-up interval.[28] Hahn et al showed that the average volume of the ablation zone was reduced by 75% at the one-year mark with a patient satisfaction rate of 96%.[29] Another study by Golatta et al assesses outcomes of cryoablation in fibroadenomas ≤3 cm and found that 93% were nonpalpable at one year with a patient satisfaction rate of 97%.[30] Reported adverse events in these studies were minor, including localized skin changes, induration, hematoma, and continued breast pain.[31,32]

Radiofrequency Ablation (RFA)— RFA utilizes a high-frequency alternating electric current administered via a probe centered in the target lesion, similar to cryoablation. The electric current heats adjacent tissue water molecules causing coagulation. Water molecules are more prevalent in neoplastic tissue compared to healthy surrounding tissue.[32] Furthermore, neoplastic vessels are abnormal and more susceptible to the coagulative effects as compared to healthy vasculature. These characteristics combine to cause preferential ablation of abnormal tissue. In RFA, a 1-cm margin of tissue is required around the lesion, limiting its use for lesions near the skin, chest wall, or breast implants.[32] Most literature regarding RFA centers around breast carcinoma and many consider it the most promising ablation modality for breast cancer with good long-term outcomes.[33] Studies investigating RFA for fibroadenoma are limited.[32] However, small studies have shown success. Teh et al reported on RFA treatment of 2 patients with fibroadenoma, both of whom had complete clinical and technical success at 6-month follow-up.[34] Further investigation to better delineate the role of RFA in fibroadenoma treatment is required.

Laser Ablation— In laser ablation a thin fiber is inserted percutaneously under either ultrasound or MRI guidance. Low-power laser light energy is delivered via the fiber, which heats the surrounding tissues. Tumor necrosis depends on exposure time and tissue temperature.[31] Tissue temperatures can be followed by MR thermometry or with internal temperature monitors.[32] The area and shape of the necrosis is difficult to predict due to biologic variability, fiber tip charring, and changing optical and thermal properties of the tissue during laser photocoagulation.[31] Only a few studies have used this technique for fibroadenoma treatment. While this technique boasts quick treatment times and success rates comparable to fibroadenoma cryoablation in the few studies performed, there were more frequent complications, notably skin breakdown and pain.[31] As a result, it is not widely implemented in clinical practice.

High-Intensity Focused Ultrasonography (HIFU)— This is a relatively new, completely noninvasive ablative technique in which an ultrasound beam generated by a piezoelectric transducer is focused on the target tissue under either MRI guidance (MRgFUS) or ultrasound guidance.[31,32] The ultrasound beam propagates through tissue as a high-energy pressure wave that heats target tissue to 60-95°C causing protein denaturation and coagulative necrosis without impacting surrounding healthy tissue.[31] This technique has shown success in breast cancer treatment, and phase II clinical trials are ongoing.[32] HIFU is also being investigated as a treatment for fibroadenoma. Hynynen et al treated 11 fibroadenomas with MRgFUS and had technical success of 72%, defined as partial or complete nonenhancement on follow-up MRI.[35] An additional study by Kovatcheva et al showed a volume reduction of 72.5% at a 12-month follow-up.[36] Other studies are ongoing with further patient

follow-up required. While promising, more research into applications of this technique for fibroadenoma is necessary.

Conclusion

Fibroadenomas are common breast masses, especially in women under age 30. The imaging features of fibroadenoma overlap with multiple other benign and malignant breast masses. As such, fibroadenomas account for a large proportion of breast biopsies. Cosmesis is a central concern when treating fibroadenomas given the benignity and patient population. Open surgical excision remains the most common treatment choice. However, multiple minimally invasive techniques, notably ultrasound-guided percutaneous cryoablation, have been utilized to effectively treat fibroadenoma with improved cosmetic outcomes as well as other advantages including cost effectiveness, lack of general anesthesia risks, and increased patient comfort.

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Abnormal Placentation as a Cause for Vaginal Bleeding in Pregnancy

Irene Vasko, D.O.,[1] Chandni Bhimani, D.O.,[2] Pauline Germaine, D.O.[1]

[1] Department of Radiology, Cooper University Hospital, Camden, NJ
[2] Department of Radiology, Thomas Jefferson University Hospital, Philadelphia, PA

Case Presentation

A 36-year-old G3P2002 woman at 26 weeks and 6 days' gestational age (GA) with a history of two prior cesarean sections, presented to a labor and delivery department with vaginal bleeding. Due to an abnormal prenatal ultrasound, the patient recently underwent fetal MRI for further evaluation of ultrasound findings **(Figures A-D).** Upon presentation, fetal and maternal vital signs were stable. During the observation period, the patient developed persistent contractions despite magnesium sulfate administration. She subsequently was taken to the operating room at 28 weeks' GA for a third cesarean section.

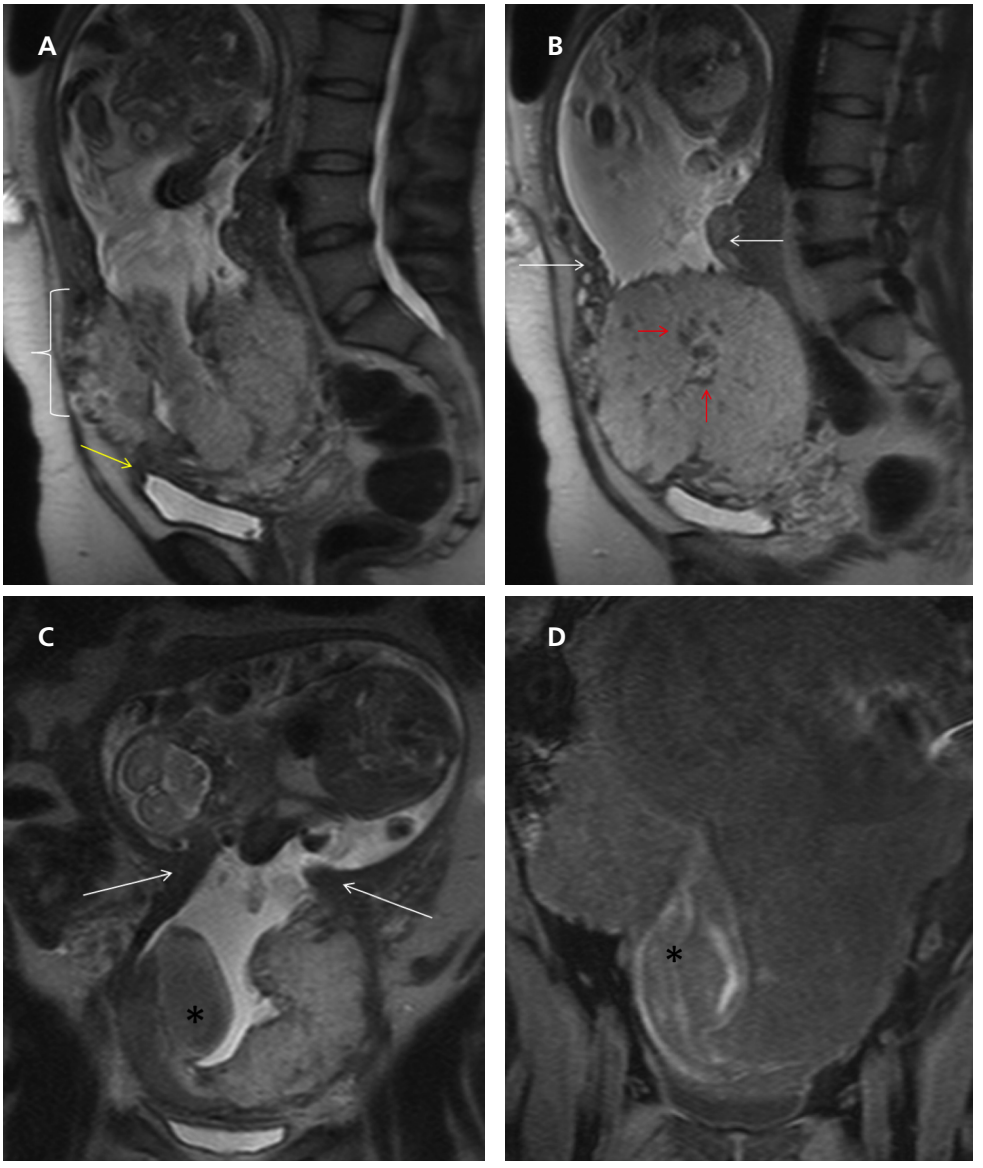

FIGURE 1. *Unenhanced MRI of the pelvis with attention to the gravid uterus obtained at 26+1 weeks' gestational age: (A,B) sagittal T2 half-Fourier acquisition single-shot turbo spin-echo (HASTE), (C) coronal T2 HASTE and (D) coronal T1 fat-saturated volumetric interpolated breath-hold examination (VIBE). (A) A focal bulge is identified in the anterior lower uterine segment at the level of placental implantation with focal areas of disruption of the normal outer myometrium (white bracket) and focal tenting of the urinary bladder at the dome (yellow arrow). (B, C) The uterus has an hourglass configuration (white arrows) and thick low T2 signal intraplacental bands (red arrows in B). (C, D) Heterogeneous T2 hypointense and T1 hyperintense collection in the lower uterine segment represents a hematoma (black asterisks).*

Differential Diagnosis

Placenta previa
Morbidly adherent placenta
(accreta vera/increta/percreta)
Vasa previa
Placental abruption

Discussion

A normal placenta is discoid in shape, 2-4 cm thick and is embedded within the anterior, posterior or fundal uterine wall at least 2 cm from the internal cervical os.[1,2] On MRI, the placenta has a homogenous, intermediate T2 signal with clear distinction from the adjacent myometrium and smooth linear regions of hypointensity throughout. The myometrium is characterized by 3 distinct layers on T2-weighted sequences: thin hypointense inner and outer layers with a thicker intermediate signal middle layer. These layers become more difficult to differentiate as the myometrium thins with progression of pregnancy. The gravid uterus is normally smooth in contour with the uterine fundus greater in diameter in relation to the lower uterine segment.[3]

Placenta previa and morbidly adherent placenta (MAP), previously known as placenta accreta spectrum, are key differential diagnoses of abnormal placentation. Prevalence of these conditions has been increasing in the United States alongside increasing numbers of cesarean sections.[3] Intact decidua basalis tissue is necessary for normal placentation; therefore, any prior trauma predisposes a pregnant woman to placental abnormalities. The risk factors for both placenta previa and MAP are prior cesarean sections or other uterine surgery including myomectomy, dilatation and curettage, in addition to congenital uterine anomalies and advanced maternal age.[3,4] Initial ultrasound diagnosis is usually made at 18 to 20 weeks' gestation with further MR imaging indicated in challenging or equivocal cases, such as if the placenta is difficult to visualize secondary to a poor acoustic window, overlying bowel gas and/or placental positioning. Additionally, MRI offers superior soft-tissue contrast that is helpful in surgical planning of confirmed cases of MAP. [1-3,5]

Placenta Previa

Implantation of the placenta within the lower uterine segment near the internal cervical os results in a low-lying marginal placenta or placenta previa. The two conditions are within the same spectrum with distinction made by the proximity of the placental edge to the internal os. A low-lying placenta is within 2 cm of the os while full extension over the os defines previa.[4] Ultrasound is diagnostic, although an increased rate of false positives is seen during the second trimester of pregnancy as the placenta shifts during the third trimester with increased uterine distention.[2]

Morbidly Adherent Placenta

MAP encompasses a spectrum of abnormal chorionic villi invasion into the myometrium. The spectrum consists of accreta vera, the mildest and most common form, with limited superficial invasion of the myometrium; increta, defined by further extension into the myometrium; and percreta, the most severe form, with penetration of both the myometrium and serosa, and potential extension into adjacent structures. Clinical diagnosis is usually made at delivery, at which time placental detachment fails, resulting in bleeding and potential need for a hysterectomy. Other severe complications include disseminated intravascular coagulopathy, acute respiratory distress syndrome (ARDS), renal failure and even death.[3] MR imaging is highly sensitive and specific for the diagnosis of MAP, providing pertinent anatomic detail that can optimize patient management by planning the ideal timing and location of delivery, need for interdisciplinary involvement and/or availability of blood products. Additionally, intrapartum diagnoses can prepare the patients and their families for potential complications with significant future implications.[2,3]

The imaging findings associated with the spectrum of MAP utilize the knowledge of normal appearance of the placenta to identify the different aspects of abnormal placentation. As stated, the myometrium has distinct layers and signal intensities; MAP causes interruption of the smooth utero-placental interface with focal defects and thinning of the layers, particularly the outermost layer. This finding unfortunately can be difficult to detect if the myometrium is diffusely thinned secondary to pregnancy progression; it is also nonspecific in regions of prior cesarean section scar tissue. In contrast, thick T2 hypointense intraplacental bands are highly sensitive for MAP.[2,3,6] Although the pathophysiology of the finding is not completely known, it is thought to relate to fibrin deposition secondary to hemorrhage, with increased band volume and heterogeneity corresponding to the increasing degree of invasion.[3] The placenta can also be abnormally thickened with increased vascularity; this results in increased flow voids on T2 imaging. The abnormal vessels measure at least 6 mm in diameter and have corresponding hyperintensity on balanced steady-state free precession (SSFP) sequences, secondary to vessel hypertrophy.[3]

An irregular uterine contour with focal bulging and deviation from the normal pear-like shape, is highly indicative of placental invasion. This abnormal uterine configuration consists of widening of the lower uterine segment, creating an "hourglass" uterus.[2] Additionally, loss of definite tissue planes adjacent to the myometrium indicates placenta percreta. As the placenta infiltrates through the uterine serosa, the bladder becomes the most frequent target for further invasion. The key imaging feature for this diagnosis is urinary bladder wall tenting.[2,3,6]

Vasa Previa

Vasa previa is associated with high fetal mortality rates (approximately 60%) and is defined by abnormal fetal vessels overlying the internal cervical os.[7] The vessels are unsupported by the umbilical cord or the placenta and are vulnerable to tearing, especially upon rupture of membranes.[8] Painless vaginal bleeding is the presenting symptom,

with an incidence rate of 1:2,500 and an alarmingly high fetal mortality rate secondary to massive fetal hemorrhage; prenatal diagnosis of the condition is key for appropriate management and surgical planning.[7,8] It is divided into 2 types: type I in which there is a single placental lobe with a velamentous umbilical cord (cord insertion into the chorioamniotic membrane instead of the placenta), and type II, with multiple placental lobes with connecting vessels that cross the internal os.[7]

The presence of tubular or round anechoic structures with corresponding flow on color Doppler overlying the cervix on transvaginal ultrasound examination is diagnostic; however, further evaluation with MRI may be indicated in equivocal cases.[8] MRI can additionally assess for placental variations, such as the number of lobes and their locations to aid in surgical planning of confirmed cases. Specifically, time-of-flight magnetic resonance angiography (MRA) performed without intravenous contrast can provide more detailed information as to the type of vasa previa and the vascular distribution.[7-9]

Placental Abruption

Placental abruption is the premature detachment of the placenta from the myometrium resulting in hemorrhage and possibly fetal death. Associated risk factors include maternal trauma, vascular disease, chorioamnionitis and cocaine use. Hemorrhage may occur within the placental parenchyma or be adjacent. If hemorrhage is adjacent to the placenta it is further characterized as being retroplacental (on the maternal side) or subchorionic (on the fetal side). Imaging is necessary for accurate diagnosis. Although ultrasound may be able to diagnose abruption, it has low sensitivity and cannot visualize the full extent of hemorrhage, particularly if massive. In the setting of maternal trauma, CT of the abdomen and pelvis is the study of choice due to the life-threatening nature of the diagnosis. On CT, there may be areas of full-thickness placental hypoenhancement and/or an adjacent hyperattenuating hematoma. MRI is less frequently performed in nonemergent cases due to duration of the study; findings are those of hemorrhage with variable signal characteristics depending on the acuity of the abruption.[1]

Diagnosis

MAP/placenta percreta

Summary

Formation of a normal utero-placental interface is a critical component of a successful pregnancy and delivery. Abnormal location or extent of implantation leads to significantly increased rates of maternal and fetal morbidity and mortality.[2,4] Placenta previa, morbidly adherent placenta (formerly placenta accreta spectrum), vasa previa and placental abruption are direct consequences of abnormalities within the utero-placental interface and result in significant fetal/neonatal and maternal morbidity and mortality due to peripartum and postpartum hemorrhage and possible emergent hysterectomy.[3] Early identification of abnormally adherent placentation is necessary as multispecialty management is often necessary. Ultrasound remains the primary means of diagnosis. MR imaging serves as a complementary exam to ultrasound in cases of potential abnormally adherent placentation, and is useful if sonographic findings are equivocal or if the placenta is posteriorly located.[2,5] An accurate imaging diagnosis with ultrasound and fetal MRI can greatly improve fetal and maternal outcomes.

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Suspicious Thyroid Nodule in Pregnancy

Sameh Neamaalla, M.D., Eman Kalboush, M.D., Maria Solis, M.D.

Department of Radiology, Cooper University Hospital, Camden, NJ

Case Presentation

A 25-year-old, 6-months' pregnant woman presented with hypothyroidism and a thyroid nodule. She had a prior fine-needle aspiration (FNA) of a right-sided nodule with benign results, but on follow-up ultrasound, the nodule had enlarged **(Figure 1 A, B)**.

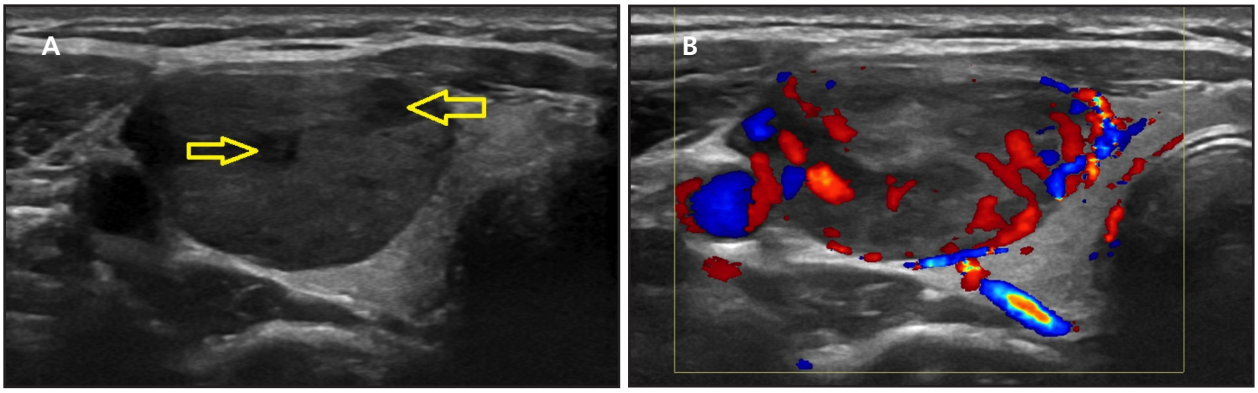

FIGURE 1. *Thyroid nodule in a 25-year-old pregnant woman. Transverse sonogram of the right lobe of the thyroid gland. (A) Circumscribed, hypoechoic solid nodule and internal cystic component (yellow arrows) without surrounding hypoechoic halo. (B) Color Doppler sonogram shows increased internal vascularity.*

Key Clinical Findings

Fatigue, constipation, dry skin and neck lump during pregnancy

Key Imaging Findings

Enlarging solitary mixed solid and cystic nodule in the right thyroid lobe

Differential Diagnosis

Papillary carcinoma
Follicular carcinoma
Medullary carcinoma
Anaplastic carcinoma

Discussion

Thyroid nodules are a common clinical problem. Given the typical pregnant patient demographics and frequent physician encounters during pregnancy, it is not surprising that incidental thyroid nodule workups are common during pregnancy. The radiologist should be prepared to be part of the workup of thyroid nodules and their subsequent management. Although many thyroid nodules are benign, thyroid cancer is common.[1] Approximately 10% of thyroid cancers that occur during the child-bearing period are diagnosed during pregnancy or in the first year after birth.[2]

According to the American Thyroid Association (ATA), the optimal diagnostic approach for a thyroid nodule detected during pregnancy is comprehensive history, physical examination, serum thyroid-stimulating hormone (TSH) and thyroid ultrasound. FNA is indicated according to the level of suspicion defined by ultrasonographic features. Calcitonin measurement may be performed in pregnant women with a family history of medullary thyroid carcinoma, MEN 2 or a known RET gene mutation. Radionuclide scintigraphy or radioiodine uptake determination is contraindicated during pregnancy.[3]

The American College of Radiology (ACR) Thyroid Imaging Reporting and Data System (TI-RADS) committee has proposed ultrasound-based risk stratification systems to identify nodules that warrant biopsy or sonographic follow-up. Other societies, such as the ATA, have taken a slightly different, pattern-oriented approach, but with the same intent. Although the ACR TI-RADS recommendations provide guidance, radiologists and referring physicians are obligated to use clinical judgment in every case. The decision to perform FNA should also account for the referring physician's preference and the patient's risk factors for thyroid cancer, anxiety, comorbidities, life expectancy, and other relevant considerations.[4]

Although the workup and decision to biopsy is no different between pregnant and nonpregnant patients, the management for a patient diagnosed with malignancy is different. The management is largely based on the histopathology, and whether the malignancy is considered well-differentiated. It is crucial that a multidisciplinary approach be taken involving pathology, radiology (nuclear medicine), obstetrics/gynecology, endocrinology, anesthesiology, and surgery when providing a patient with accurate information and guiding management. The 2017 ATA clinical guidelines aid management of thyroid cancer in pregnancy.[3]

For patients diagnosed with differentiated (papillary and follicular) thyroid cancer, there are options about whether to begin treatment during pregnancy vs after delivery. If surgery is considered while the patient is pregnant, timing is critical. Surgery could be safely performed during the second trimester or delayed until delivery without worsening prognosis. Thyroidectomy performed during the first trimester carries a risk of teratogenicity or may increase the risk of miscarriage.[3] In the third trimester, there is a high risk of premature labor and potential hypotension due to vena cava compression by the uterus in the supine position, which may cause fetal hypoperfusion.[3]

In contrast to well-differentiated thyroid cancer, delaying surgery until delivery can adversely affect the outcome in pregnant women with newly diagnosed medullary carcinoma or anaplastic cancer. After clinical assessment, surgery should be strongly considered.[3]

The need for radioactive iodine (RAI) therapy depends on the cell type and risk but must wait until after pregnancy. RAI should only be administered if a woman has a negative pregnancy test 72 hours before treatment is given. RAI is also significantly concentrated in lactating breast tissue. Therefore, RAI should not be given to breastfeeding women. Breastfeeding should stop at least 6 to 8 weeks prior to radioiodine therapy to reduce radioiodine uptake by breast tissue.[5]

At 6 months' postsurgery, a neck ultrasound should be performed and serum thyroglobulin should be monitored closely during the first year after thyroid surgery. Additional neck ultrasound and other imaging modalities such as diagnostic radioiodine whole-body scan, MRI, CT and F-18 fluorodeoxyglucose (FDG) PET/CT are tailored according to the patient's risk of recurrence.[5]

Overall prognosis and survival rates in patients diagnosed with thyroid cancer during pregnancy are not significantly different from that in nonpregnant women with similar disease.[1]

Papillary Carcinoma

Papillary carcinoma is the most common type of thyroid cancer and frequently has lymph node involvement at presentation. It is more common in women with a peak incidence in the third and fourth decades.[6] On ultrasound, papillary carcinoma usually

appears as a single, solid hypoechoic nodule with cystic component and ill-defined margins. The nodule can contain microcalcifications (psammoma bodies) in the form of punctate echogenic foci without posterior acoustic shadowing. On color Doppler, there is increased internal vascularity. Lymph node metastasis tends to cavitate.[6]

Follicular Carcinoma

Follicular carcinoma represents 2% to 5% of thyroid cancers. It can occur in a pre-existing microfollicular or macrofollicular adenoma. Lymph node metastasis in follicular carcinoma is rare. However, hematogenous spread is more common at presentation.[6] On ultrasound, it is typically a homogenously hypoechoic nodule without cystic change. Color Doppler shows extensive internal flow with or without a peripheral ring.[6] The definitive diagnosis of follicular carcinoma is made by thyroidectomy.

Medullary Carcinoma

Medullary carcinoma accounts for about 5% of thyroid malignancy. It occurs sporadically and in a familial form as a component of multiple endocrine neoplasia type II syndrome.[6] It is characterized by production of calcitonin. On ultrasound, it is a hypoechoic nodule with coarse shadowing calcifications. Involved lymph nodes also contain calcifications.[6]

Anaplastic Carcinoma

Anaplastic carcinoma is a highly aggressive thyroid cancer with peak incidence in the sixth to seventh decades. It carries the worst prognosis.[6] Patients usually present late with obstructive symptoms such as dyspnea, dysphagia, and laryngeal nerve palsy. On ultrasound, it appears as an ill-defined infiltrative mass demonstrating necrosis and dense amorphous calcifications with internal flow on color Doppler. The involved nodes are hypoechoic and necrotic. Extracapsular spread with infiltration of the trachea, esophagus, and perithyroid soft tissues is common.[6]

Diagnosis

Papillary thyroid carcinoma

Summary

Thyroid nodules occur often in young women and can be discovered during pregnancy. The decision to biopsy is no different than in a nonpregnant woman. However, if thyroid cancer is diagnosed during pregnancy, surgery can be delayed to after delivery for papillary and follicular carcinoma. Delaying surgery for poorly differentiated thyroid cancer may adversely affect prognosis. Radioactive iodine is contraindicated during pregnancy and lactation. The management of thyroid cancer in pregnancy is complicated and requires a solid multidisciplinary team approach, which may need referral to a larger medical center with experience and resources to handle such cases.

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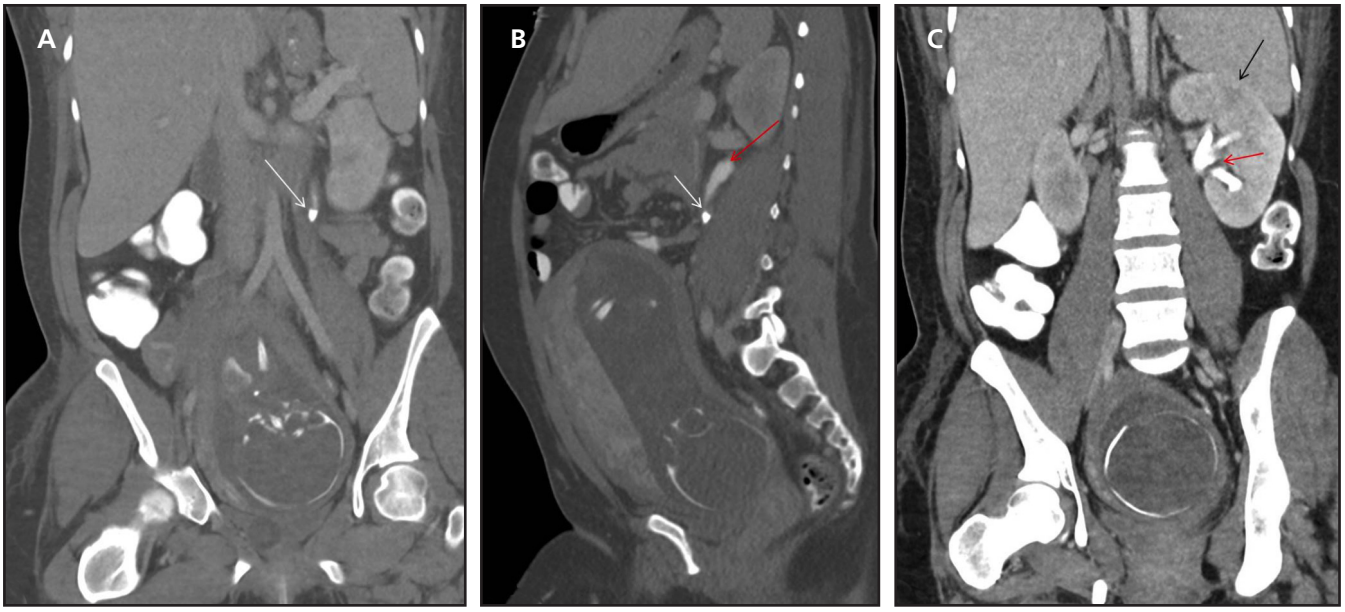
JAOCR at the Viewbox

Irene Vasko, D.O., Pauline Germaine, D.O.

Department of Radiology, Cooper University Hospital, Camden, NJ



Obstructive Uropathy in Pregnancy

A 23-year-old G1P0 woman, at 26+0 weeks' gestational age, was admitted with abdominal and lower back pain with suspected nephrolithiasis. The patient subsequently became febrile, tachycardic and had a rise in serum creatinine. A contrast-enhanced CT of the abdomen and pelvis was performed showing a 0.5-cm calculus within the proximal left ureter **(white arrow, A)** with mild hydronephrosis and delayed persistent excretion of contrast that was administered for a chest CT the preceding day **(red arrow, B C).** The left renal parenchyma was heterogeneously enhancing **(black arrow, C)**, suggestive of postobstructive edema vs pyelonephritis. The patient's hospital course was complicated by pyelonephritis and septicemia, for which she underwent placement of a left double-J stent and subsequent lithotripsy.

The incidence of urolithiasis in pregnancy is approximately 1:2000;[1] however, it is the most frequent cause of nonobstetric abdominal pain. Anatomic and physiologic contributing factors lead to urolithiasis during pregnancy, such as ureteral compression by the gravid uterus and smooth muscle relaxation secondary to high progesterone levels. These factors lead to gestational hydronephrosis, causing urinary stasis and promoting calculus formation.

Ureteral obstruction is a complication that can further lead to acute kidney injury, pyelonephritis, urosepsis and premature labor, conditions that are life-threatening to the mother and fetus.[1] Imaging is a key component in achieving a prompt and accurate diagnosis. An ultrasound of the kidneys and bladder is the first-line study in evaluation of nephrolithiasis in pregnancy, posing no risk to the fetus. It, however, has both low sensitivity and specificity in the pregnant patient.[1] The second-line imaging study is a CT of the abdomen and pelvis without contrast. Although there is exposure of the fetus to radiation, CT is the most sensitive and specific exam with an almost 100% renal calculus detection rate,[1] and should be performed if diagnosis cannot be made with ultrasound, or if the patient clinically deteriorates. There is increasing clinical interest in using MR over CT for evaluation of ureteral obstruction as it avoids radiation, but interpretation may be challenging as the stones, particularly if small and nonobstructing, may be difficult to visualize due to low signal intensity on most pulse sequences.[1,2]

Initial management of urolithiasis in pregnancy is conservative, with use of analgesics and hydration to promote spontaneous passage of the calculus. This approach can only be utilized in uncomplicated cases.[2] If the patient has signs of infection or fails conservative management, temporizing intervention is indicated, with placement of a ureteral stent or percutaneous nephrostomy. Definitive treatment with lithotripsy is preferably performed postpartum, but in cases that require definitive treatment during pregnancy, ureteroscopic lithotripsy is recommended.[1,2]

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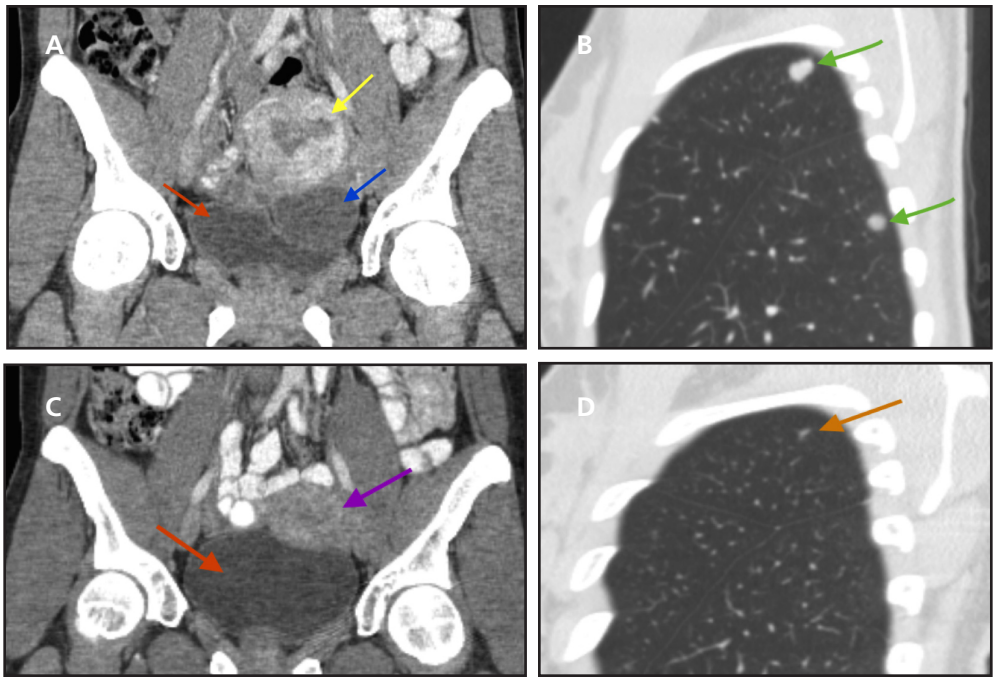
JAOCR at the Viewbox

Kimberly Klinger, M.D., M.S.H.A., Christopher Roth, M.D., M.S.H.Q.S

Department of Radiology, Thomas Jefferson University Hospital, Philadelphia, PA



Gestational Trophoblastic Disease (GTD)

A 29-year-old G5P1A3 female with positive β-hCG presented for an initial dating fetal ultrasound. Ultrasound showed a complex, heterogeneous intrauterine collection and no live pregnancy. She underwent dilation and evacuation with pathology showing a complete mole. Her β-hCG remained elevated and uptrending. She underwent staging CT and repeat dilation and evacuation.

Contrast-enhanced CT of the abdomen and pelvis (**A**) showed heterogeneous endometrial thickening and enhancement (yellow arrow) and a left adnexal cystic structure (blue arrow) causing mass effect on the normal urinary bladder (red arrow). Initial CT of the chest (**B**) showed multiple well-defined lung nodules (green arrows). She was treated with methotrexate alternating with leucovorin and β-hCG downtrended. Post-treatment contrast-enhanced CT of the abdomen and pelvis (**C**) showed resolution of the left adnexal cystic structure and associated mass effect on the bladder (red arrow) and decreased endometrial thickening and enhancement (purple arrow). Follow-up CT of the chest (D) showed decrease in size and near complete resolution of multiple pulmonary nodules compared with pretreatment imaging with a few small residual nodules remaining (orange arrow).

Gestational trophoblastic disease (GTD) is a spectrum of benign and malignant tumors, including hydatidiform mole, invasive mole, choriocarcinoma, placental site trophoblastic tumor, and epithelioid trophoblastic tumor. Those with potential to metastasize are referred to as gestational trophoblastic neoplasia (GTN).[1,2]

Ultrasound is the primary imaging modality for evaluation and diagnosis of GTD in correlation with clinical findings and β-hCG levels. The role of CT is limited to staging in patients with suspected GTN.[1,2] On contrast-enhanced CT, moles are seen as irregular, low-attenuating intrauterine masses with thin enhancing septations.[1,2] Enlarged ovaries containing multiple cysts ("spoke-wheel" appearance) are also seen due to gonadotrophin hyperstimulation.[1,2] Approximately 30% of patients with GTN have metastases at the time of diagnosis, most commonly to the lungs.[1] The most frequent thoracic manifestation of metastatic disease are multiple well-defined, solid lung nodules.[1]

Nonmetastatic GTN and low-risk metastatic GTN treated with single-agent chemotherapy have cure rates approaching 100%.[1] Patients classified as having high-risk metastatic disease treated with multi-agent chemotherapy with or without adjuvant radiation therapy or surgery have cure rates of 80% to 90%.[1]

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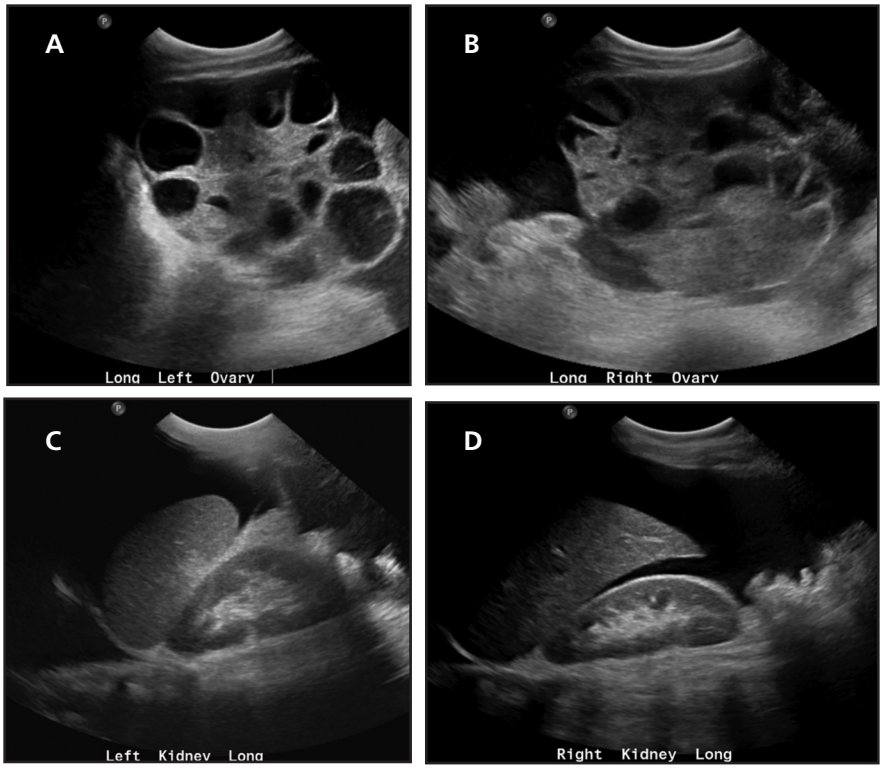
JAOCR at the Viewbox

Kimberly Klinger, M.D., M.S.H.A., Evan Rochlis, M.D.

Department of Radiology, Thomas Jefferson University Hospital, Philadelphia, PA



Ovarian Hyperstimulation Syndrome (OHSS)

A 28-year-old G0P0 woman who had been taking fertility medications for the past 15 days and underwent egg retrieval one day ago presented with increasing abdominal pain and distention. Pelvic ultrasound (US) showed markedly enlarged ovaries bilaterally with multiple cysts (**A, B**) and normal vascularity. There was free fluid in the abdomen and pelvis, some of which was hemorrhagic, and bilateral pleural effusions (**C, D**).

Ovarian hyperstimulation syndrome (OHSS) is an iatrogenic condition that occurs due to increased capillary permeability following the administration of exogenous hormones for ovarian stimulation as part of assisted reproduction. It occurs most commonly following hCG administration but can rarely occur with clomiphene or GnRH. Risk factors include young age, low body weight, polycystic ovarian syndrome, high doses of exogenous hormones, high or rapidly rising estrogen, and prior OHSS.[1] The syndrome is self-limited; however, it can be severe and life threatening due to complications such as renal failure, respiratory distress, and thromboembolism.

Bilateral, symmetrically enlarged ovaries containing multiple variably sized cystic lesions ("spoke wheel" appearance) representing enlarged follicles or corpus luteum cysts in the presence of ascites are the typical imaging findings.[2] Corpus luteum cysts and ascites can be echogenic on US or dense on CT from hemorrhage. Additional imaging findings that can be seen on US, CT or MRI include pleural effusion and thromboembolism.

The modified Golan Classification is commonly used to measure the severity of OHSS and divides OHSS into mild, moderate, and severe based on ovarian sizes of < 6 cm, 6-12 cm, and > 12 cm, respectively.[2] Other imaging features considered in the Golan classification are the presence of ascites, thrombosis, and/or hydrothorax.

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