Multiple Circumscribed Fibroadenomas in a Single Quadrant of the Breast: A Case Report with Imaging-Pathology Correlation

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AUTHOR CONTRIBUTIONS

Vigneshkumar Palanisamy: The author was responsible for the conception, design, data collection, imaging review, manuscript writing, and final approval of the submitted version.

Deepti Dissanayake: The Author helped with data collection, imaging review, analysis.

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Yes

HUMAN AND ANIMAL RIGHTS

None

ABSTRACT

Fibroadenoma is a common benign breast tumor typically presenting as a solitary, well-circumscribed mass in younger women. Although multiple fibroadenomas are not uncommon, they are typically distributed bilaterally and scattered throughout the breast tissue. In this report, we describe the rare presentation of multiple fibroadenomas clustered within a single quadrant of one breast in a perimenopausal woman, identified during routine screening. Diagnostic imaging revealed several circumscribed, hypoechoic nodules without suspicious features. Histological evaluation following targeted biopsies confirmed all lesions as benign fibroadenomas. This case illustrates an uncommon imaging pattern of a common lesion and highlights the importance of imaging—pathology correlation in guiding appropriate clinical management.

CASE REPORT

BACKGROUND

Fibroadenomas represent the most common benign tumors of the breast, typically arising from a proliferation of both epithelial and stromal components of the terminal duct lobular unit. Their development is strongly influenced by hormonal factors, especially estrogen, and they frequently present in young women during their reproductive years [1]. Although fibroadenomas are generally solitary, multiple lesions can occur in up to 15–20% of cases. These are most often bilateral and scattered. The occurrence of multiple fibroadenomas confined to a single breast quadrant, however, is exceedingly rare and underreported in the literature.

Histopathologically, fibroadenomas are considered biphasic neoplasms, composed of benign ductal epithelium and a fibrous stroma, and can mimic or overlap with other fibroepithelial lesions such as phyllodes tumors [2]. While fibroadenomas are not typically associated with an increased risk of breast cancer, their presence may be confounded with other proliferative or atypical lesions, requiring careful differentiation [3]. Phyllodes tumors, in particular, share several overlapping imaging and histologic features and can exhibit aggressive behavior if not accurately identified [4].

The diagnostic challenge intensifies in perimenopausal or

Journal of Radiology Case Reports

postmenopausal women where new fibroadenomas are less common, and imaging findings may raise suspicion for more ominous pathologies. As demonstrated by Guray and Sahin, a thorough evaluation of benign breast diseases requires nuanced clinical, radiological, and pathological correlation, especially when the presentation deviates from classic norms [5].

Furthermore, the role of hormone replacement therapy (HRT) has been explored in the context of breast tissue proliferation. Estrogen-only HRT, commonly prescribed to women with a history of hysterectomy, has been shown to stimulate fibroglandular tissue, potentially contributing to the persistence or new formation of fibroadenomas beyond the reproductive age [6].

This case is significant because it presents a rare diagnostic scenario: multiple clustered fibroadenomas in a single breast quadrant of a perimenopausal woman receiving estrogen therapy, with no associated symptoms or malignancy risk factors. It reinforces the value of multimodal imaging, imageguided biopsy, and multidisciplinary discussion in accurately diagnosing benign but unusual presentations, thus avoiding unnecessary surgical interventions.

CASE REPORT

A 55-year-old perimenopausal woman presented for her eighth routine biennial screening mammogram under the BreastScreen WA program. She reported no breast-related complaints at the time of screening. Her past medical history included a right total knee reconstruction performed six months earlier, an ovary-sparing hysterectomy, and a prior left oophorectomy for ovarian cysts. Her medication list included magnesium, vitamin D, fish oil supplements, and hormone replacement therapy presumed to be estrogen-only. She was also taking venlafaxine for vasomotor symptoms. She had no personal or family history of breast or ovarian cancer. She reported an allergy to iodine-based contrast agents and was otherwise in good health.

The patient had undergone a cosmetic breast reduction and abdominoplasty in 2005. She was gravida 3, para 3, with her first pregnancy occurring at the age of 18. All three of her children were breastfed briefly. She did not smoke and consumed alcohol occasionally in social settings. On clinical breast examination, there was no dominant mass or skin change. However, nodularity was noted in the lower outer quadrant of the left breast. There was no axillary lymphadenopathy, and the nipple–areolar complexes were unremarkable bilaterally. The right breast was clinically and radiologically unremarkable.

Screening mammography of the left breast demonstrated a 75 mm area of multiple small, well-defined, rounded densities in the lower outer quadrant. A targeted ultrasound of the left breast showed five clustered, well-circumscribed, hypoechoic lesions in the 4 o'clock position, with the largest measuring 11 mm in transverse diameter. These lesions were closely approximated,

had no evidence of posterior shadowing or enhancement, and did not demonstrate internal vascularity on Doppler interrogation. A solitary, similarly appearing lesion measuring 8 mm was also identified in the 5 o'clock position of the same breast. No additional suspicious lesions or cysts were noted, and there was no sonographic evidence of axillary lymphadenopathy or retro areolar pathology.

Given the unusual appearance of multiple clustered nodules in a single quadrant, two of the lower outer quadrant lesions were selected for ultrasound-guided core needle biopsy on October 2, 2024. The anterior lesion was designated as lesion 1A and the posterior as lesion 1B. Both returned histopathology consistent with benign fibroadenomas, with no evidence of atypia or malignancy. Although reassuring, the imaging findings raised the possibility of heterogeneity among the clustered lesions, prompting discussion at a multidisciplinary breast conference. The consensus was to further sample the lesion located in the upper outer quadrant to exclude any radiologically occult pathology. A stereotactic tomosynthesis-guided core needle biopsy of this 10 mm lesion was performed on October 16, 2024, and histological examination once again confirmed a benign fibroadenoma.

After review of the imaging and pathology results, the lesions were considered radiologically and histologically concordant. The patient was informed of the benign nature of all three biopsied masses and was advised to remain breast aware and report any new or persistent changes. She was discharged back to primary care with a recommendation for a temporary one-year rescreen through BreastScreen WA. Should no interval changes be detected on the subsequent imaging, she would return to the standard biennial surveillance schedule.

DISCUSSION

Etiology & Demographics

Fibroadenoma is the most common benign tumor of the breast in women, accounting for approximately 50% of total breast biopsy performed in females under 30 years of age and occurring in up to 10% of the female population [1,2]. These tumors usually emerge during the reproductive age and are closely associated with hormonal activity, especially estrogen. Histologically, fibroadenomas are biphasic neoplasms comprising both epithelial and stromal components, and they are generally considered to arise from aberrant lobular development under hormonal stimulation [3].

Although fibroadenomas are frequently solitary, multiple fibroadenomas can be found in 15–20% of patients, with bilateral distribution being the most common pattern [4]. However, the presentation of clustered fibroadenomas restricted to a single quadrant of one breast, particularly in a perimenopausal woman, is exceedingly rare. In a large retrospective series, such localized clustering was reported in less than 1% of all fibroadenoma cases [5]. The rarity of this condition poses diagnostic challenges, as such a pattern may mimic multifocal neoplastic processes.

The patient in this report was 55 years old, placing her outside the typical age range for new fibroadenoma formation. However, her use of estrogen-only hormone replacement therapy may have contributed to the development or persistence of the lesions, as hormonal therapy has been associated with continued stromal proliferation in select individuals beyond menopause [6].

Clinical & Imaging Findings

Clinically, fibroadenomas are usually asymptomatic, slow-growing, and mobile on palpation. They are often discovered incidentally during imaging studies or routine physical examinations. In the present case, the patient exhibited no clinical symptoms but was found to have nodularity in the lower outer quadrant of the left breast during a routine screening examination. Mammography identified a 75 mm cluster of small masses in the same region. Ultrasound examination revealed multiple oval, well-circumscribed, hypoechoic nodules with no internal vascularity and horizontal orientation, features consistent with benign fibroadenomas [7].

A solitary 10 mm lesion was also noted in the upper outer quadrant of the left breast on digital breast tomosynthesis. Given the multiplicity and distribution of lesions, a targeted biopsy approach was employed. Two lesions from the lower quadrant and one from the upper quadrant were biopsied using ultrasound and tomosynthesis-guided techniques, respectively. Histopathology confirmed all lesions as benign fibroadenomas. Radiologic—pathologic concordance was established, and the absence of atypical features further reduced the suspicion of malignancy.

The imaging findings in this case align with the classic ultrasonographic and mammographic presentations of fibroadenomas. According to Stavros et al., fibroadenomas typically appear as oval or gently lobulated masses with circumscribed margins and demonstrate homogeneous internal echotexture without posterior shadowing or enhancement [8]. Tomosynthesis has been shown to increase lesion conspicuity, particularly in dense or previously operated breasts, and was instrumental in the full assessment of this patient's mammographic abnormalities [9].

Treatment & Prognosis

Journal of Radiology Case Reports

Management of fibroadenomas depends on lesion size, growth pattern, imaging features, patient age, and personal preference. In patients with classic imaging features and confirmed benign histology, surveillance is the standard of care. Excision is reserved for symptomatic lesions, those with rapid growth, atypical histological features, or patient preference [10].

The prognosis for fibroadenomas is excellent. They are not considered premalignant, although the risk of malignant transformation exists in rare cases—estimated at less than 0.3% in large longitudinal studies [11]. Additionally, the risk of developing breast cancer is not significantly increased in patients with simple fibroadenomas unless associated with complex features or proliferative disease on histology [12].

In this case, the patient was appropriately managed with non-operative follow-up and was advised to undergo a one-year rescreen before returning to standard biennial surveillance. This approach is consistent with best-practice guidelines, particularly when the imaging and pathology findings are in agreement and the clinical context does not raise concern for underlying malignancy.

Differential Diagnoses

The clustered nature of the lesions necessitated consideration of alternative diagnoses. Phyllodes tumors represent the most significant diagnostic mimic, particularly in their benign form. They may initially present with imaging features similar to fibroadenomas but tend to grow rapidly and may demonstrate irregular margins or internal heterogeneity. Phyllodes tumors account for less than 1% of all breast neoplasms, and their incidence is approximately 2.1 per million women annually [13].

Pseudoangiomatous stromal hyperplasia (PASH) is another benign proliferative entity that may appear as a mass-forming lesion on imaging. PASH can be hormonally responsive and often affects premenopausal or perimenopausal women. On histology, it is characterized by dense collagenous stroma with slit-like spaces mimicking vascular channels, a feature absents in our biopsies [14].

Hamartomas, also known as lipofibroadenomas, are benign lesions composed of varying proportions of fat, glandular, and fibrous tissue. Their classic "breast within a breast" appearance on mammography usually facilitates diagnosis. In contrast, lipomas are purely adipose lesions and typically appear radiolucent on mammography and hypoechoic on ultrasound. Sclerosing adenosis and intraductal papilloma's may also enter the differential but are more commonly associated with calcifications or ductal changes [15].

Intraductal papilloma is another important differential consideration for circumscribed breast lesions [16]. It often presents with ductal changes such as focal ductal asymmetry or associated microcalcifications on mammography, and may appear as an intraductal mass on ultrasound, occasionally with ductal dilation. Unlike fibroadenomas, intraductal papilloma's may be associated with nipple discharge or pain [17]. On MRI, these lesions typically show iso- to hyperintense signal on T2-weighted images and may demonstrate variable contrast enhancement depending on their vascularity and epithelial activity. In the present case, the absence of ductal dilation, retroareolar pathology, or associated calcifications made intraductal papilloma unlikely, and it was excluded based on

imaging and biopsy findings [18].

Given the consistent imaging features, benign biopsy results, and multidisciplinary consensus, these alternate diagnoses were effectively excluded in this case. The confirmation of fibroadenomas at three distinct sites within the breast, coupled with the absence of any suspicious clinical or imaging findings, supported a conservative management strategy without further intervention.

TEACHING POINT

Clustered fibroadenomas can mimic multifocal malignant lesions on imaging, particularly when confined to a single quadrant and appearing as multiple well-circumscribed, hypoechoic nodules. Recognition of their characteristic ultrasound and mammographic features, combined with appropriate image-guided biopsy, is essential to avoid overdiagnosis and unnecessary intervention.

OUESTIONS

Question 1: Which of the following answer choices is false regarding typical ultrasound features of fibroadenomas?

- 1. They are well-circumscribed and hypoechoic.
- 2. They display oval morphology and horizontal orientation.
- 3. They demonstrate internal vascularity on Doppler. (applies)
- 4. They lack posterior acoustic enhancement or shadowing.
 - 5. They are generally avascular and homogeneous.

Explanation:

- 1. Fibroadenomas are usually oval and hypoechoic with smooth margins. ["The classic sonographic appearance... includes a well-circumscribed, oval shape and hypoechoic echotexture."]
- 2. They lie parallel to the skin and exhibit horizontal alignment. ["They commonly demonstrate horizontal orientation to the skin."]
- 3. Internal vascularity is not typical and may suggest an alternative diagnosis such as phyllodes tumor. ["They generally lack internal vascularity on Doppler interrogation."]
- 4. Fibroadenomas typically do not display significant posterior acoustic features. ["These lesions... had no evidence of posterior shadowing or enhancement."]
- 5. Homogeneous echotexture is a common benign characteristic. ["Uniform echogenicity across the lesions further supported a benign etiology."]

Question 2: Which of the following conditions should be included in the imaging-based differential diagnosis of multiple circumscribed breast lesions?

- 1. Phyllodes tumor (applies)
- 2. Pseudoangiomatous stromal hyperplasia (applies)
- 3. Fat necrosis
- 4. Hamartoma (applies)

5. Intraductal papilloma (applies)

Explanation:

- 1. Phyllodes tumors can resemble fibroadenomas on imaging, especially in early stages. ["Phyllodes tumors... can present with similar imaging features in early stages."]
- 2. PASH may mimic fibroadenomas, particularly when nodular. ["Pseudoangiomatous stromal hyperplasia... may also mimic fibroadenomas on imaging."]
- 3. Fat necrosis usually has irregular margins or calcifications and is not typically confused with fibroadenomas.
- 4. Hamartomas may show a "breast within a breast" appearance but can present as circumscribed masses. ["Hamartomas represent another potential mimic... circumscribed margins aid in their distinction."]
- 5. Intraductal papilloma can appear as solid masses on imaging. ["Other less common considerations include lipomas, adenosis, and papilloma's..."]

Question 3: Which of the following statements about fibroadenoma epidemiology is true?

- 1. They are most common in postmenopausal women.
- 2. Multiple fibroadenomas occur in 50% of patients with fibroadenomas.
 - 3. They are more frequently seen in males.
- 4. They occur most often between the ages of 15 and 35 (applies)
- 5. They are typically associated with malignant transformation.

Explanation:

- 1. Fibroadenomas are less common after menopause. ["Most common in women aged 15–35 years; uncommon in postmenopausal women..."]
- 2. Multiple fibroadenomas occur in approximately 15–20% of cases. ["Multiple fibroadenomas occur in 15–20% of affected individuals..."]
- 3. They are exceedingly rare in males. ["Predominantly female; extremely rare in males."]
- 4. They most frequently occur during the reproductive years. ["Most common in women aged 15–35 years..."]
- 5. Risk of malignant transformation is extremely low (<0.3%). ["...risk of malignant transformation is very low (<0.3%)."]

Question 4: Which of the following are valid clinical indications for the surgical excision of a fibroadenoma?

- 1. Rapid interval growth (applies)
- 2. Imaging-histology concordance with benign features
- 3. Patient preference despite benign histology (applies)
- 4. Small, asymptomatic lesion with stable appearance
- 5. Concordant benign lesion in a postmenopausal woman on hormone therapy

Explanation:

1. Rapid growth is one of the main clinical reasons to consider excision, as it may raise suspicion for phyllodes tumor or atypia. ["Surgical excision is typically reserved for fibroadenomas demonstrating rapid growth, discordant

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imaging-pathology findings, or atypia..."]

- 2. Imaging–histology concordance supports conservative follow-up, not surgery.
- 3. Even if benign, patient anxiety or cosmetic concerns may justify excision. ["Excision may also be considered based on patient preference..."]
- 4. Conservative management is preferred for stable, small, asymptomatic lesions.
- 5. Postmenopausal status alone does not necessitate excision if findings remain benign and concordant.

Question 5: Which of the following statements accurately reflects findings from the presented case?

- 1. The lesions were confined to the left breast quadrant. (applies)
 - 2. Biopsy revealed malignant phyllodes tumor.
- 3. The patient had a significant family history of breast cancer.
 - 4. All lesions were vascular and irregular.
 - 5. Follow-up imaging was not recommended.

Explanation:

- 1. All lesions were localized to the lower and upper outer quadrants of the left breast. ["...multiple clustered fibroadenomas confined to a single breast quadrant..."]
- 2. Histopathology confirmed benign fibroadenomas. ["Histopathology confirmed all sampled lesions as benign fibroadenomas."]
- 3. There was no family history of breast or ovarian cancer. ["She reported no significant family history of breast or ovarian cancer."]
- 4. Lesions were circumscribed, avascular, and benign on imaging. ["...well-circumscribed, hypoechoic lesions... with no internal vascularity."]
- 5. A one-year rescreen was recommended. ["... recommended a temporary one-year re-screen at BreastScreen WA."]

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FIGURES



Figure 1: Mediolateral oblique (MLO) mammogram of the left breast demonstrates a 75 mm region of multiple, closely clustered, oval-to-round dense nodules located in the lower outer quadrant (circled). These correspond to biopsy sites 1A and 1B—marked with anterior twirl and posterior HydroMARK clips—and are consistent with fibroadenomas. No microcalcifications, skin thickening, or axillary lymphadenopathy is identified.

TECHNIQUE: Digital screening mammogram acquired on 14 September 2024 using a SIEMENS Mammomat Revelation unit. View: Left breast, MLO. Breast thickness: 83 mm. Image resolution: 4095 x 2048. Settings: 200 mAs, 50 kVp. No contrast or magnification was used. Image was de-identified for submission.

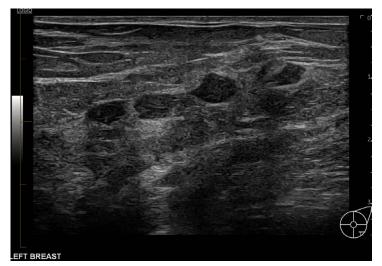


Figure 2: Transverse grayscale ultrasound image of the left breast shows five closely clustered, well-circumscribed, hypoechoic solid masses without internal vascularity, located at the 4 o'clock position, corresponding to the region of concern seen on mammography. The lesions measure up to 11 mm in the transverse plane and demonstrate no associated posterior acoustic enhancement or shadowing.

TECHNIQUE: High-frequency linear probe ultrasound using GE LOGIQ system, ML6-15 transducer, 14 MHz, gain 60, performed on 02/10/2024. No contrast administered.

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Summary table: Key Characteristics of Multiple Fibroadenomas

Category	Details	
Etiology	Benign proliferation of both stromal and epithelial components of the terminal duct lobular unit, influenced by hormonal stimulation (especially estrogen).	
Incidence	Occurs in approximately 10% of women; multiple fibroadenomas occur in 15–20% of these cases.	
Gender Ratio	Predominantly female; extremely rare in males.	
Age Predilection	Most common in women aged 15-35 years; uncommon in postmenopausal women unless on hormone replacement	
	therapy.	
Risk Factors	Young age, family history of benign breast disease, estrogen therapy, reproductive hormone fluctuations, obesity.	
Treatment	Observation if asymptomatic and confirmed benign; surgical excision if rapidly enlarging, symptomatic, or atypical on imaging or histology.	
Prognosis	Excellent; negligible risk of malignant transformation (<0.3%) for simple fibroadenomas.	
Findings on Imaging	Well-circumscribed, oval, hypoechoic masses with parallel orientation on ultrasound; round or oval, homogeneous	
	density on mammography; no vascularity on Doppler.	

This summary table outlines the essential clinical, epidemiologic, and imaging characteristics of multiple fibroadenomas, with emphasis on benignity and diagnostic approach.

Differential table: Imaging Features of Circumscribed Breast Lesions

Diagnosis	Imaging Modality	Findings
Fibroadenoma	Mammography	Oval, circumscribed, homogeneous density
	Ultrasound (US)	Well-defined, hypoechoic, oval, horizontal orientation, no internal vascularity
	MRI T1	Isointense
	MRI T2	Mildly hyperintense
	MRI DWI	No restricted diffusion
	Contrast Enhancement	Minimal or no enhancement
	PET/Scintigraphy	No increased uptake
Phyllodes Tumor	Mammography	Lobulated, denser lesion; coarse calcifications possible
	Ultrasound (US)	Irregular, heterogeneous, internal vascularity present
	MRI T1	Iso- to hyperintense
	MRI T2	Hyperintense
	MRI DWI	May show restricted diffusion
	Contrast Enhancement	Avid, heterogeneous
	PET/Scintigraphy	Moderate uptake possible
	Mammography	"Breast within a breast" appearance (fat and soft tissue components)
	Ultrasound (US)	Mixed echogenicity (fatty and glandular tissue)
Hamartoma	MRI T1	Visible fat components
	MRI T2	Mixed signal
	Contrast Enhancement	Mild heterogeneous enhancement
	PET/Scintigraphy	No significant uptake
PASH Intraductal Papilloma	Mammography	May appear dense, non-specific
	Ultrasound (US)	Hypoechoic mass or diffuse stromal thickening
	MRI T1	Isointense
	MRI T2	Slightly hyperintense
	Contrast Enhancement	Mild to moderate
	PET/Scintigraphy	No increased uptake
	Mammography	Ductal asymmetry or microcalcifications
	Ultrasound (US)	Intraductal mass, may cause duct dilation
	MRI T1	Isointense
	MRI T2	Hyperintense
	Contrast Enhancement	Variable; can show enhancement
	PET/Scintigraphy	Variable activity depending on cellular activity

This differential table outlines key radiologic features across modalities for fibroadenoma and similar benign breast lesions. It supports accurate differentiation and appropriate diagnostic workup.

KEYWORDS

Fibroadenoma; Benign breast tumor; Clustered breast nodules; Breast ultrasound; Digital breast tomosynthesis; Breast neoplasm differential; Terminal duct lobular unit

ABBREVIATIONS

MRI = MAGNETIC RESONANCE IMAGING

US = ULTRASOUND

DWI = DIFFUSION WEIGHTED IMAGING

CT = COMPUTED TOMOGRAPHY

PET = POSITRON EMISSION TOMOGRAPHY

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