Occult Breast Cancer Presenting as Isolated Axillary Lymphadenopathy: A Case Report with MRI–Pathology Correlation

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CONSENT
(No consent due to no patient identifiers used.)

HUMAN AND ANIMAL RIGHTS
(No human/animal experiments were performed)

ABSTRACT

Occult breast cancer is a rare presentation of invasive ductal carcinoma in which axillary lymph node metastasis is identified without a detectable breast lesion on mammography or ultrasound. We report a case of a 57-year-old woman recalled from screening mammography for bilateral breast asymmetries that resolved on diagnostic compression views. Targeted ultrasound of the axillary revealed a solitary lymph node with progressive cortical thickening. Core needle biopsy demonstrated metastatic carcinoma, consistent with mammary origin. Breast MRI subsequently localized enhancing foci, confirmed as invasive ductal carcinoma. This case highlights the diagnostic value of contrast-enhanced breast MRI in identifying otherwise occult primary breast tumors and correlation of imaging and histopathologic findings in establishing a definitive diagnosis in clinical occult presentations.

CASE REPORT

BACKGROUND

Occult Breast Cancer (OBC) is a rare form of breast carcinoma, accounting for less than 1% of all cases. OBC is defined by axillary lymph node metastasis without a primary breast lesion on mammography or ultrasound. Most OBCs are later diagnosed as invasive ductal carcinoma (IDC) on histopathology. True diagnosis often requires the use of contrast-enhanced breast MRI to identify occult primaries. The case highlights how isolated axillary lymphadenopathy is the only manifestation of a breast primary, the importance of MRI in detecting small occult lesions and the value of pathologic correlation in confirming mammary origins.

CASE REPORT

A 57-year-old woman was recalled from routine screening mammography for evaluation of bilateral breast asymmetry. A diagnostic mammogram was performed for the bilateral breast asymmetries which resolved on additional spot compression images. They were compatible with summation of normal fibroglandular tissue (Figure A). The patient had no personal or family history of breast or ovarian cancer.

Ultrasound of the left axilla demonstrated a single lymph node with focal cortical thickening measuring 0.7 cm (Figure B). Other normal nodes were also noted. The contralateral right

axilla was imaged for comparison and showed normal nodes. Ultrasound of the left whole breast was performed to ensure no suspicious findings to account for the left unilateral axillary adenopathy and no findings were identified. Given the isolated adenopathy, a two month follow up using Breast Imaging Reporting and Data System (BI-RADS) 3 recommendation was used to observe changes to the left axillary lymph node.

At two month follow up, the cortical thickening of the left axillary lymph node progressed to 0.8 cm (Figure B). Ultrasound guided core needle biopsy was then recommended and performed. Flow cytometry revealed no diagnostic features of a lymphoproliferative neoplasm. Yet, histology exhibited metastatic carcinoma involving the lymph nodes positive for cytokeratins AE1/AE3 and GATA3 while negative for transcription factor SOX10. Estrogen receptor (ER) was positive (>90% moderate nuclear staining). Progesterone receptor (PR) was positive (49% moderate nuclear staining). Human epidermal growth factor receptor 2 (HER-2) neu score was negative. The proliferation index (Ki-67) was 6% nuclear staining.

Mammography and ultrasound of the breasts remained negative for a primary tumor, Magnetic Resonance Imaging (MRI) was performed with and without contrast to identify the precise site of primary carcinoma and for breast surgeon consultation. Axial post-contrast images showed two masses with an intervening 2.6 x 0.9 x 0.8 cm non-mass enhancement forming linear distributions in the left breast (Figure C). Sagittal post-contrast sequence revealed suspicious sites of primary breast malignancy, designated lesion A and Lesion B. Lesion A is a 0.7 cm irregular enhancing mass at the 10:00 position, 7 cm from the nipple and Lesion B is a 0.8 cm irregular enhancing mass at the 11:00 position, 9 cm from the nipple (Figure C).

MRI guided biopsies were performed for both enhancing foci of the left breast. Lesion A biopsy yielded only fibroadipose tissue with blood, without evidence of malignancy or atypia. Lesion B biopsy and histopathologic analysis of the specimen demonstrated invasive ductal carcinoma, grade 1, measuring 4 mm in greatest dimension. Immunohistochemical studies showed the tumor cells to be positive for CK7, with p63 and calponin expression supporting the diagnosis of invasive carcinoma. The tumor exhibited strong membranous E-cadherin staining, supporting ductal phenotype.

DISCUSSION

Etiology & demographics

Occult breast cancer (OBC) without a detectable primary tumor in the breast is rare, accounting for less than 1% of all breast cancer diagnosis [1,2]. OBC is defined as metastatic carcinoma consistent with breast origin in the axillary lymph nodes without an identifiable primary lesion in the breast on mammography or ultrasound. Most occult primary cancers are later proven histologically to be invasive ductal carcinoma (IDC), which remains the predominant subtype of invasive breast malignancy, accounting for 80% of cases [2].

OBC remain mammographically and sonographically occult due to their small size, retroareolar or deep parenchymal location [3,4]. Breast MRI, with its superior contrast resolution, has dramatically improved the detection of clinically silent primary lesions, identifying up to 80% of patients previously considered “occult” [4,5].

OBC typically affects women between ages 50-70 years of age, paralleling the demographic distribution of conventional IDC [4]. Like other breast cancers, OBC shares established risk factors including prolonged estrogen exposure, family history of breast cancer, BRCA1/2, nulliparity, and late menopause [4,5].

Clinical & imaging findings

Mammography

No suspicious calcification, architectural distortion, or focal asymmetries were identified. OBC often presents with axillary lymphadenopathy in the absence of a palpable breast mass or abnormality on routine breast imaging.

Whole breast ultrasound

Whole-breast ultrasound revealed no masses, cystic lesion, or suspicious shadowing. A solitary axillary lymph node with cortical thickening measuring 0.7 cm, which progressed to 0.8 cm at follow-up, warranting biopsy.

MRI

Contrast enhanced subsequently revealed two irregular enhancing masses in the left breast, Lesion A, measuring 0.7 cm at the 10:00 position and Lesion B, measuring 0.8 cm at the 11:00 position. The presentation of the lesions are consistent with a single disease process spanning approximately 2.6 x 0.9 x 0.8 cm. No abnormal enhancement was identified in the contralateral breast.

Core Needle Biopsy Results

Metastatic carcinoma involving lymph node tissue. Immunohistochemistry showed CKAE1/AE3 (+) and GATA3 (+), SOX10 (-).

ER (+, >90% moderate nuclear staining), PgR (+, 49% moderate nuclear staining), HER2 neu (-, score 0), Proliferation Index (Ki-67): 6%.

Results confirmed a low-proliferative, hormone receptor-positive, HER2 negative phenotype, most consistent with invasive ductal carcinoma. The abnormal axillary lymph node biopsy demonstrated metastatic carcinoma, establishing that the axillary nodal metastasis originated from an undetected breast carcinoma.

MRI Histopathology Results

Lesion A, located at the 10:00 position, yielded fibroadipose tissue with blood and no evidence of malignancy or atypia.

Lesion B, located at the 11:00 position, revealed invasive ductal carcinoma, grade 1, measuring 4 mm in maximum dimension. Immunohistochemical analysis demonstrated tumor cells positive CK7, p63 and calponin, supporting the diagnosis of invasive carcinoma. Strong membranous E-cadherin staining supports a ductal epithelial phenotype, consistent with invasive ductal carcinoma.

Treatment & prognosis

Management of OBC follows the same principle as IDC, with treatments guided by tumor biology, receptor status, and extent of nodal metastasis [4]. In patients initially presenting with axillary metastasis of unknown primary cancer, therapy is directed toward controlling both axillary and primary breast sites. Traditionally, modified radical mastectomy with axillary dissection was the standard approach. However, breast conserving therapy (whole-breast irradiation combined with axillary lymph node dissection) demonstrates comparable survival outcomes [6]. Given the tumor's hormone receptor (ER+/PR+/HER2-), and low-proliferative (Ki-67 6%) profile, endocrine therapy often is the main choice of adjuvant treatment, accompanied by selective estrogen receptor modulators (SERM) or aromatase inhibitors [7].

The overall prognosis for OBC parallels that of non-occult invasive ductal carcinoma when treated appropriately, with a 5-year overall survival rate exceeding 90% [4,6]. Favorable outcomes of OBC are strongly linked to hormone receptor positivity, low proliferation index, and limited nodal metastasis, all of which the present case exhibits.

Differential Diagnoses

The differential diagnosis for isolated axillary lymphadenopathy with negative breast imaging is broad, and both malignant and benign etiologies must be considered. The key diagnostic challenge in OBC is distinguishing metastatic mammary carcinoma from non-mammary malignancies and inflammatory conditions.

In the present case, immunohistochemical analysis is crucial in narrowing the differential. The lymph node biopsy demonstrated metastatic carcinoma with CKAE1/AE3 (+), GATA3 (+), and SOX10 (-), confirming breast origin and excluding metastatic melanoma and other non-mammary adenocarcinomas [8]. Negative flow cytometry ruled out lymphoproliferative disease processes such as lymphoma. From an imaging standpoint, the American College of Radiology (ACR) Appropriateness Criteria recommends contrast-enhanced breast MRI as the next diagnostic step for patients with axillary metastasis and negative mammography and ultrasound [9]. MRI offers the highest sensitivity for detecting invasive tumors occult on conventional imaging.

Prior to immunohistochemical confirmation, the differential diagnosis for isolated axillary lymphadenopathy that should be considered are occult breast carcinoma, metastatic non-mammary adenocarcinoma and lymphoma. Benign possibilities include reactive lymphadenopathy or sarcoidosis.

Occult breast carcinoma remains the leading diagnosis in adult women with unilateral axillary metastasis and no apparent breast lesion. MRI demonstrates a small enhancing mass or area of non-mass enhancement within the ipsilateral breast, while CT may show asymmetric axillary node enlargement with preserved fat hilum [10]. Histologically, OBCs are typically low grade, with nests of atypical epithelial cells.

Metastatic lung adenocarcinoma and thyroid carcinoma can metastasize to the axillary node. Lung adenocarcinoma typically demonstrates multiple spiculated pulmonary nodules with mediastinal adenopathy on CT. Thyroid carcinoma metastases present with high T2 signal on MRI, reflecting colloid and cystic changes [11]. Metastatic ovarian or endometrial carcinoma may show enhancing soft tissue nodules on MRI and peritoneal or omentum disease on CT [12]. Histologically, lung adenocarcinoma is characterized by gland forming epithelial cells with mucin production, showing TTF-1 (+) and Napsin A (+) [11].

Lymphoma (Both Hodgkin or non-Hodgkin) can mimic metastatic nodal disease, often presenting with bilateral, symmetric nodal enlargement. On MRI, lymphoma demonstrates intermediate T1 and hyperintense T2 signals with moderate homogenous enhancement. CT reveals homogeneously enhancing soft tissue masses without necrosis [13]. Lymphoma is composed of sheets of atypical lymphoid cells, with immunoreactive markers for CD20 (B-cell lineage) or CD3 (T-cell lineage).

Sarcoidosis CT may show clustered, non-necrotic lymph nodes with perilymphatic distribution, while tuberculosis can appear with central necrotic, rim-enhancing nodes with high T2 signal intensity. Sarcoidosis is a benign mimic of OBC characterized by noncaseating granuloma, with associated CD68 (+) and elevated serum ACE levels [14].

TEACHING POINT

Occult breast cancer should be considered in patients presenting with isolated axillary lymphadenopathy and no detectable lesions on mammography or ultrasound. Breast MRI is the most sensitive modality for identifying a hidden primary tumor.

QUESTIONS

Question 1: Which of the following best defines occult breast cancer (OBC)?

A. A breast malignancy identified only at autopsy
B. A breast lesion smaller than 7 mm on MRI

C. A metastatic carcinoma in the axillary lymph node without a detectable breast primary tumor on mammography or ultrasound (applies)
D. A carcinoma confined to the nipple-areolar complex
E. A diffuse skin thickening of the breast

Explanation for question 1

OBC is defined as metastatic carcinoma in axillary lymph nodes with no identifiable breast lesion on mammography or ultrasound. MRI often localizes the hidden primary focus.

["Occult breast cancer is defined as metastatic carcinoma in axillary lymph nodes without an identifiable breast primary on conventional imaging."]

Question 2: Which immunohistochemical profile supports a mammary origin of metastatic carcinoma?

A. TTF-1 (+), Napsin A (+), GATA3 (-)
B. CD20 (+), CD3 (+), CD19 (-)
C. CKAE1/AE3 (+), GATA3 (+), SOX10 (-) (applies)
D. S100 (+), HMB-45 (+), GATA3 (+)
E. PAX8 (+), WT-1 (+), ER (-)

Explanation for question 2

Breast primaries show epithelial differentiation with CKAE1/AE3 and GATA3 positivity and SOX10 negativity, distinguishing them from melanoma, lung adenocarcinoma, or lymphoma. ["The carcinoma was CKAE1/AE3 (+) and GATA3 (+) while SOX10 (–), consistent with a mammary primary."]

Question 3: Which imaging modality has the highest sensitivity for detecting primary lesions in OBC?

A. Mammography
B. Ultrasound
C. PET/CT
D. Contrast-Enhanced breast MRI (applies)
E. Chest X-Ray

Explanation for question 3

MRI provides the greatest sensitivity (up to 80–90%) for identifying small, retroareolar, or posteriorly located invasive foci not visible on mammography or ultrasound.

["MRI offers the highest sensitivity for detecting invasive tumors that are occult on conventional imaging."]

Question 4: What is the most common histological subtype identified in patients with OBC?

A. Invasive lobular carcinoma
B. Medullary carcinoma
C. Invasive ductal carcinoma (applies)
D. Mucinous carcinoma
E. Apocrine carcinoma

Explanation for question 4

Most occult breast cancers are found to be invasive ductal carcinoma upon histologic evaluation. ["Most occult primaries are later proven histologically to be invasive ductal carcinoma, which remains the predominant subtype."]

Question 5: Which of the following entities may mimic OBC on imaging and should be included in the differential diagnosis?

A. Metastatic lung adenocarcinoma (applies)
B. Lymphoma (applies)
C. Sarcoidosis (applies)
D. Fibroadenoma
E. Thyroid goiter

Explanation for question 5

Metastatic lung adenocarcinoma, lymphoma, and sarcoidosis can all present with axillary adenopathy. Distinction relies on histopathology and immunohistochemistry.

["Differential considerations include metastatic non-mammary adenocarcinoma, lymphoma, and sarcoidosis."]

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FIGURES

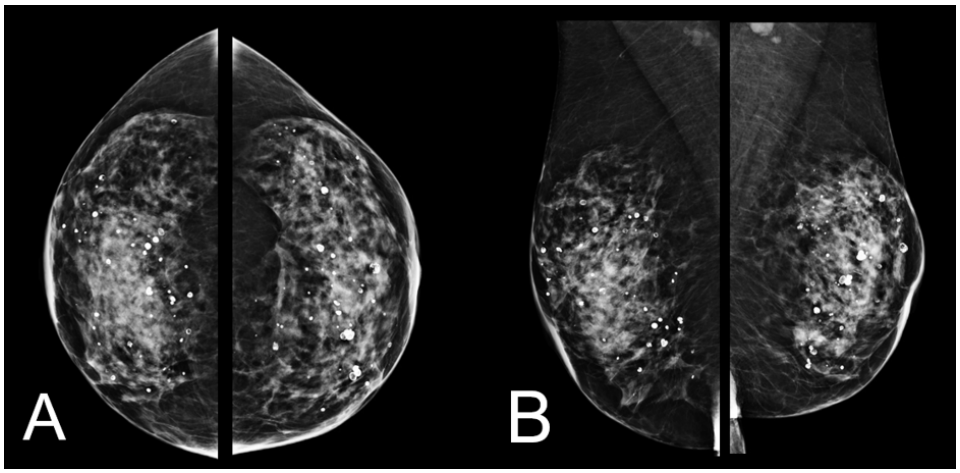

Figure A: (Left) Bilateral Cranialcaudal (CC) projections of screening mammography and (Right) Bilateral Mediolateral Oblique (MLO) Projection of screening mammography demonstrating heterogenous dense fibroglandular tissue without suspicious masses, calcification, or architectural distortions. Findings are consistent with BI-RADS 1 (negative screening study) prior to the discovery of isolated axillary lymphadenopathy.

Technique: Full-field 2D digital mammography with standard CC and MLO projections.

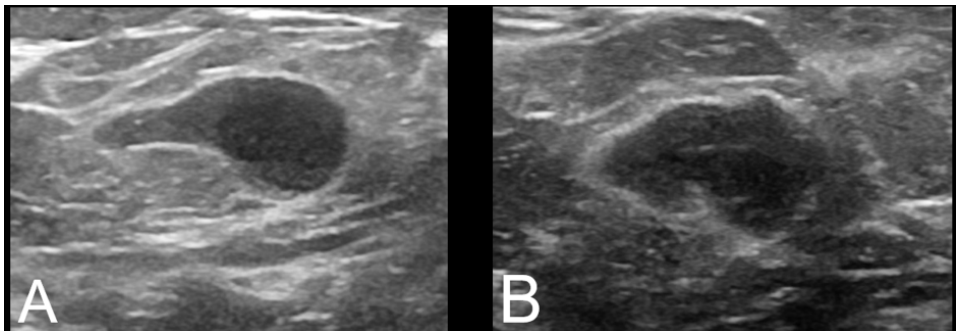

Figure B: Targeted left axillary ultrasound demonstrating progressive cortical thickening of an isolated lymph node.

(A) Initial ultrasound demonstrates a solitary oval lymph node with a cortical thickening of 0.7 cm. (B) Two month follow up ultrasound shows progressive nodal involvement, demonstrating cortical thickening to 0.8 cm with slight attenuation of the fatty hilum. These findings prompted ultrasound-guided core needle biopsy, which revealed a metastatic process.

Technique: High frequency linear transducer (12-15 MHz) using grayscale sonography of the left axilla.

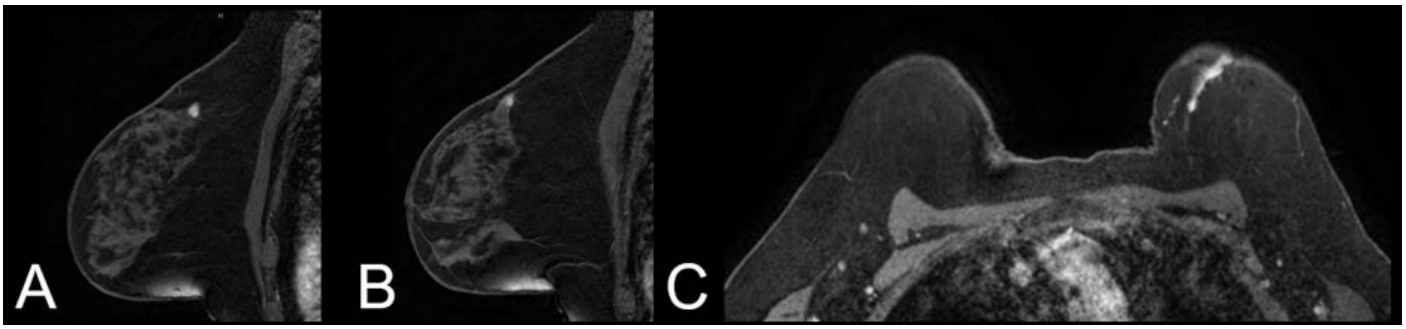

Figure C: (A) Sagittal T2-weighted image of the left breast at the 10:00 position, small irregular focal hyperintensity measuring 0.7 cm. (B) Sagittal T2-weighted image of the left breast at the 11:00 position, demonstrating a 0.8 cm focal hyperintensity. (C) Axial T2-weighted post contrast images showing two masses, intervening non mass enhancement forming linear distributions measuring 2.6 x 0.9 x 0.8 cm.

Technique: Post contrast T2-weighted fat-suppressed images acquired in the sagittal and axial planes following intravenous gadolinium.

Summary table:

Category	Details
Etiology	Malignant epithelial proliferation of ductal origin, metastatic process of the axillary node before a detectable primary breast lesion is seen on standard imaging.
Incidence	Represents <1% of all breast cancer diagnosis
Gender Ratio	Predominately female; <1% in males
Age predilection	Most commonly affects women between 50 and 70 years of age
Risk factors	Nulliparity, late menopause, family history of breast carcinoma, BRCA1/2 mutation.
Histology	Typically low grade, characterized by ductal -forming atypical epithelial cells. Tumor cells show CKAE1/AE3 (+), GATA (+), and SOX10 (-). Immunoprofile of tumor: ER(+), PrP(+), HER2(-), Ki-67 (6%)
Treatment	Surgical management with mastectomy or breast conserving therapy with axillary dissection.
Prognosis	5 year overall survival 80-90%, favorable outcomes correlate with hormone receptor positivity, low grade, and limited nodal involvement.
Imaging Finding	Mammography: Often negative or dense fibroglandular tissue. Ultrasound: may show solitary lymph node with cortical thickening. MRI: Most sensitive, reveals small enhancing or T2-hyperintensity.

Differential table:

Diagnosis	MRI Findings	CT Findings	Ultrasound Findings
Occult Breast Cancer	Small enhancing mass or linear enhancement of the ipsilateral breast.	Asymmetric axillary lymph node enlargement.	Solitary abnormal node with cortical thickening and increased vascularity.
Metastatic Lung Adenocarcinoma	Contrast enhanced T2 signal reflecting cystic changes in axillary involvement.	Spiculated pulmonary nodules or hilar adenopathy, with occasional axillary involvement.	Enlarged, hypoechoic nodes with irregular margins on axillary view.
Metastatic Thyroid Carcinoma	Contrast enhanced T2 signal reflecting cystic changes in axillary involvement.	Calcified or cystic metastatic nodes in lower neck or axilla. Associated with primary thyroid lesions.	Cystic or mixed echogenic nodes with microcalcification.
Metastatic Ovarian Carcinoma	Contrast enhanced T2 signal reflecting cystic changes in axillary involvement.	Soft-tissue nodules involving pelvic and para-aortic chains.	Solid or complex cystic nodes with vascularity.
Lymphoma	Intermediate T1 signal, hyperintense T2 signal, homogenous enhancement of lymph nodes.	Homogeneously enhancing nodal masses without necrosis.	Round, hypoechoic nodes lacking fatty hilum, typically bilateral and symmetric.
Sarcoidosis	T1 hypointense, mildly T2 hyperintense nodes with no necrosis of hilum lymph nodes.	Clustered, non-necrotic lymph nodes with perilymphatic distribution.	Multiple ovoid hypoechoic nodes with preserved hilum and minimal cortical thickening.

KEYWORDS

Occult breast cancer; Invasive ductal carcinoma; Axillary lymphadenopathy; Breast MRI; Contrast-enhanced MRI; Lymph node metastasis; Histopathologic correlation

ABBREVIATIONS

BI-RADS = Breast Imaging Reporting and Data System
CK7 = Cyto Keratin 7
CKAE1/AE3 = Cytokeratin AE1/AE3 (Broad-Spectrum Epithelial Marker)
CT = Computed Tomography
ER = Estrogen Receptor
GATA3 = GATA Binding Protein 3 (Transcription Factor Marker Of Mammary Differentiation)
HER2 = Human Epidermal Growth Factor Receptor 2
IDC = Invasive Ductal Carcinoma
Ki-67 = Cellular Proliferation Marker Ki-67
MLO = Medio Lateral Oblique (mammographic view)
MRI = Magnetic Resonance Imaging
OBC = Occult Breast Cancer
PgR / PR = Progesterone Receptor
S100 = Neural Crest And Melanocytic Marker
SOX10 = SRY-Related HMG-Box Gene 10 (Melanocytic And Neural Crest Marker)
T1 / T2 = MRI Pulse Sequences (T1-Weighted / T2-Weighted)
US = Ultra Sound

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