

Uterine and Adnexal Metastases Revealing an Occult Invasive Lobular Breast Carcinoma: A Case Report

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Abstract

Uterine metastases from breast cancer represent a rare entity, most frequently associated with invasive lobular carcinoma, which is known for its distinctive metastatic tropism. We report the case of a 60-year-old postmenopausal woman who presented with chronic pelvic pain and deterioration of general condition. Initial imaging investigations, including abdominopelvic computed tomography and pelvic magnetic resonance imaging, revealed a large uterine mass associated with ascites and diffuse bone lesions, raising suspicion of a primary uterine malignancy with metastatic spread. Further diagnostic work-up subsequently identified an invasive lobular carcinoma of the left breast with a Luminal A immunohistochemical profile. Surgical management disclosed multiple metastatic sites, including the uterus, ovaries, peritoneum, and omentum, thereby confirming the mammary origin of the lesions. This case highlights the misleading clinical and radiological presentation of gynecological metastases from invasive lobular breast carcinoma, which may closely mimic a primary gynecologic malignancy. It underscores the importance of a multidisciplinary diagnostic approach and meticulous histopathological analysis to guide optimal therapeutic management.

Keywords

Metastatic Breast Cancer, Occult Breast Cancer, Chronic Pelvic Pain, Uterine Metastasis, Breast Ultrasound-Mammography, Breast Examination, Ultrasound-Guided Biopsy, Hormone Therapy

1. Introduction

Breast cancer remains the most common malignancy among women worldwide and constitutes a major public health concern. Metastatic dissemination most frequently involves the bone, lung, liver, and brain. Gynecologic metastatic localizations, particularly uterine involvement, are exceedingly rare and represent a true diagnostic challenge from both clinical and radiological perspectives.

Invasive lobular carcinoma (ILC), although accounting for less than 10% of all breast cancers, is characterized by a distinct metastatic pattern, with a predilection for the gastrointestinal tract, peritoneum, retroperitoneum, and gynecologic organs. This behavior is largely attributed to the loss of E-cadherin expression, which disrupts cell adhesion and promotes diffuse and often insidious tumor spread.

Uterine metastases from breast cancer are uncommon, predominantly involving the myometrium, and may present either as isolated lesions or as part of widespread carcinomatosis. These metastases may mimic a primary gynecologic malignancy, leading to diagnostic delay and inappropriate therapeutic strategies. We report an original case of uterine and adnexal metastases revealing an occult invasive lobular carcinoma of the breast, aiming to highlight the clinical, diagnostic, and therapeutic specificities of this rare entity.

2. Case Presentation

A 60-year-old single, nulligravid woman with no significant past medical history, postmenopausal for 10 years, presented with chronic pelvic pain evolving over six months, associated with deterioration of general health.

Clinical examination revealed marked weight loss of 10 kg. Breast examination was unremarkable, with no palpable masses, nipple discharge, or skin abnormalities. No lymphadenopathy was detected. Gynecological examination showed an enlarged uterus on combined abdominal palpation and rectal examination (the patient was a virgin).

An externally performed abdominopelvic computed tomography scan revealed:

A uterine mass measuring 71 × 54 mm (**Figure 1**);

Diffuse axial and peripheral bone involvement suggestive of metastatic disease;

Large-volume ascites.

Pelvic magnetic resonance imaging demonstrated a suspicious endometrial tumor, radiologically assessed as FIGO stage IC, associated with significant intraperitoneal effusion and diffuse bone lesions highly suggestive of metastatic disease (**Figure 1**). This staging was considered provisional and based solely on imaging findings, with definitive staging established by postoperative histopathological examination.

Serum CA-125 level was elevated at 62.39 U/mL. Given the patient's age and the presence of secondary bone lesions, bilateral breast ultrasound combined with mammography was performed to investigate an occult breast malignancy. This examination revealed ill-defined bilateral infracentimetric nodules with suspi-

cious axillary lymphadenopathy, classified as ACR 4 in both breasts.

Breast MRI identified a 15-mm lesion in the upper inner quadrant of the left breast with suspicious ipsilateral axillary lymph nodes, classifying the left breast as ACR 5 (Figure 2), while the right breast was classified as ACR 1.

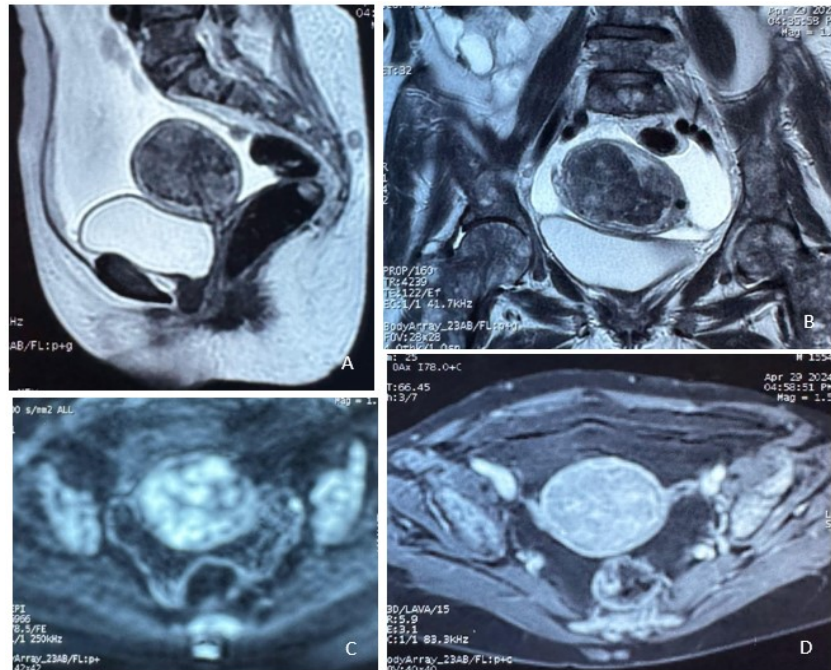
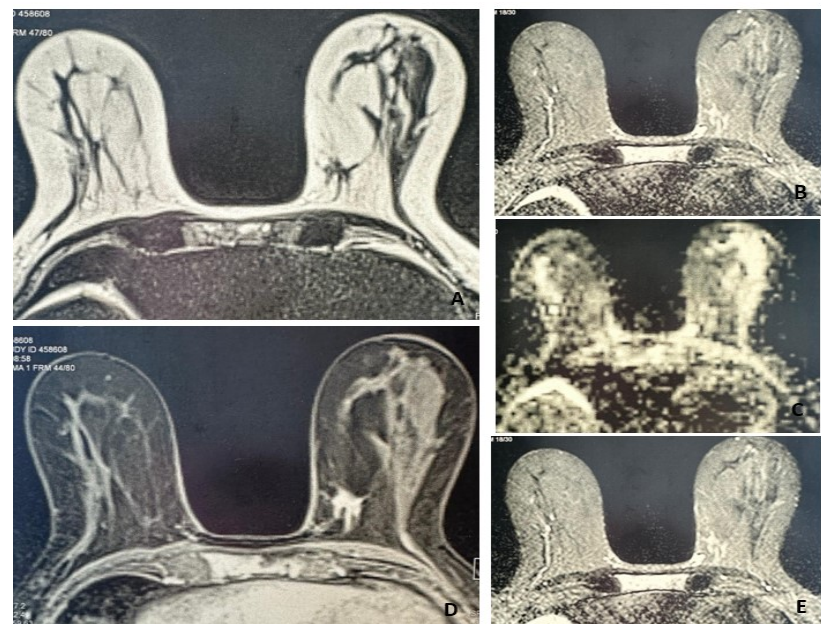


Figure 1. Abdominopelvic CT scan showing the suspicious endometrial tumor process of 71 × 54 mm classified FIGO IC.



(A) Diffusion hypersignal sequence; (B) ADC sequence; (C) T2, axial slice; (D) Injected T1, FATSAT; (E) T1 Dixon, dynamic injection.

Figure 2. 15 mm suspicious-looking nodule of the QII of the left breast, classified ACR 5.

Ultrasound-guided biopsy of the left breast lesion confirmed invasive lobular carcinoma, SBR grade II. Immunohistochemistry showed estrogen receptor positivity (80%, strong), progesterone receptor positivity (45%, moderate), Ki-67 index of 15%, HER2 negativity (score 0), consistent with a Luminal A profile.

Diagnostic hysteroscopy could not be performed due to the complete occupation of the uterine cavity by the mass. A blind endometrial biopsy revealed pseudodecidualized polypoid endocervical mucosa without evidence of malignancy on histopathological examination.

Following multidisciplinary tumor board discussion, total hysterectomy without adnexal preservation was performed, combined with left breast lumpectomy and ipsilateral axillary lymph node dissection (**Figure 3**).



Figure 3. Macroscopic image of the surgical specimens. From left to right: hysterectomy without adnexal preservation, omental biopsy, peritoneal biopsy, peritoneal fluid sampling.

Macroscopic examination of the breast specimen revealed a poorly defined, indurated grayish lesion measuring 1.2 cm. Histological analysis confirmed invasive lobular carcinoma, SBR grade II, with tumor-free margins and a focus of lobular carcinoma *in situ* (3%). Immunohistochemistry confirmed a Luminal A, HER2-negative profile. Axillary dissection revealed metastatic involvement in 9 out of 10 lymph nodes (9N+/10), with extracapsular extension.

Histological examination of the uterine specimen revealed a 6-cm intracavitary leiomyoma infiltrated by metastatic breast carcinoma. Metastatic involvement was also identified in the myometrium, fallopian tubes, ovaries, omentum, peritoneal fluid, and peritoneal biopsies. Additional immunohistochemical analysis demonstrated loss of E-cadherin expression in the uterine and other metastatic specimens, further supporting the diagnosis of metastatic invasive lobular carcinoma and confirming the mammary origin of the lesions.

Following multidisciplinary review, systemic treatment consisted of aromatase inhibitor-based hormone therapy combined with a CDK4/6 inhibitor, palliative bisphosphonates, and adjuvant breast radiotherapy. The patient is currently fol-

lowed at the oncology department of Ibn Rochd University Hospital, Casablanca.

3. Discussion

Breast cancer metastasizes via hematogenous and lymphatic routes, most commonly to the skeleton (31%), lung (19%), pleura (12%), liver (9%), brain (4%), lymph nodes (24%), local skin (22%), and distant skin (7%) [1].

Invasive lobular carcinoma, which accounts for only 9.7% of breast cancers, metastasizes more frequently to the gastrointestinal tract, gynecologic organs, and peritoneum/retroperitoneum than invasive ductal carcinoma. Borst *et al.* reported that approximately 4.5% of invasive lobular carcinomas metastasize to gynecologic organs, compared with only 0.8% of invasive ductal carcinomas [2]. Among 13 reported cases of endometrial metastases from breast cancer between 1984 and 2015, invasive lobular carcinoma was more likely to metastasize to the endometrium than invasive ductal carcinoma [3].

Uterine involvement is rare, reported in 1% - 15% of cases [4], most commonly affecting the myometrium [5], the cervix, or, more rarely, the endometrium. These metastases may occur in isolation or as part of disseminated carcinomatosis. The metastatic mechanism of breast cancer may be related to loss of E-cadherin expression on tumor cell membranes, a hallmark pathological feature of invasive lobular carcinoma. This may result from inactivation of the CDH1 gene located on chromosome 16q22 through various mechanisms, including gene mutation, chromosomal loss, and promoter methylation [5]. The loss of E-cadherin expression is a hallmark feature of invasive lobular carcinoma and plays a central role in its distinctive metastatic behavior [2]. In the present case, immunohistochemical analysis performed on the uterine and metastatic specimens confirmed the absence of E-cadherin expression, thereby supporting the proposed mechanism of diffuse tumor dissemination and reinforcing the mammary origin of the lesions.

The female reproductive system is rarely affected by metastases. The most common site is the ovary (75.8%), followed by the vagina (13.4%). Regardless of the primary tumor origin, only 8.1% of metastases involve the uterus [4]. The ovary is a highly vascularized organ with extensive lymphatic drainage and metabolic characteristics favorable to tumor implantation [6]. In contrast, the uterus contains a higher proportion of fibrous tissue, making it less conducive to tumor dissemination.

Uterine metastases may be asymptomatic or present with abnormal uterine bleeding [2], particularly when the endometrium is involved. However, chronic pelvic pain may also constitute a revealing symptom, especially when metastatic infiltration predominantly affects the myometrium or is associated with adnexal, peritoneal, or omental involvement. In such cases, pain may result from uterine enlargement, serosal irritation, or diffuse peritoneal disease rather than endometrial involvement alone. In the present case, chronic pelvic pain was the primary presenting symptom, illustrating an atypical but clinically relevant mode of presentation that may further contribute to diagnostic delay.

When tumors metastasize to the uterus, involvement is limited to the myometrium in 64.5% of cases, both myometrium and endometrium in 32.7%, and exclusively the endometrium in only 3.8% [4].

Several reports [7] [8] describe uterine metastases revealing previously undiagnosed breast cancer, further complicating diagnosis, particularly in cases of occult disease. A literature review identified 25 cases of uterine metastases, including 8 involving the myometrium, with isolated uterine involvement in 18 cases.

Ovarian metastases are often microscopic, making radiological diagnosis difficult [9] [10], which explains why imaging failed to detect ovarian involvement in our patient. Although CA-125 levels may be elevated, they do not allow localization of metastases. Diagnosis, therefore, relies exclusively on histopathological examination [11].

Given the rarity of uterine metastases from breast cancer, diagnosis and management remain challenging. Advances in systemic therapy have improved median survival in de novo stage IV metastatic breast cancer from 20 to 30 months between 1990 and 2010. The European School of Oncology Metastatic Breast Cancer Task Force recommends an aggressive, multidisciplinary approach, as a subset of patients may achieve complete remission and prolonged survival [12].

In our case, a total hysterectomy without adnexal preservation with multiple biopsies, combined with left breast lumpectomy and ipsilateral axillary dissection, was performed. Histopathological analysis confirmed metastatic involvement of the endometrium, myometrium, fallopian tubes, ovaries, ascitic fluid, and omentum. The patient subsequently received hormone therapy (aromatase inhibitors), a CDK4/6 inhibitor, bisphosphonates, and breast radiotherapy. Hormone therapy remains the cornerstone of treatment for hormone receptor-positive, HER2-negative metastatic breast cancer [13], with tamoxifen or aromatase inhibitors most commonly used [14].

The prognosis of patients with ovarian metastases from breast carcinoma is poor, with median progression-free survival ranging from 9 to 30 months, median overall survival from 16 to 38 months, and 5-year survival rates between 6% and 26% [15].

4. Conclusions

Although rare, uterine metastases from breast cancer should be considered in postmenopausal women presenting with atypical uterine masses, particularly when associated with distant metastatic lesions or deterioration of general health. Invasive lobular carcinoma, due to its biological characteristics and loss of E-cadherin expression, exhibits a unique metastatic tropism that may involve the uterus, ovaries, fallopian tubes, and peritoneum.

This case emphasizes the difficulty of preoperative diagnosis, especially in occult breast cancer, and highlights the pivotal role of histopathological and immunohistochemical analysis in identifying the primary origin of lesions. Management relies on a multidisciplinary approach combining surgery, hormone ther-

apy, systemic treatments, and adjuvant breast radiotherapy tailored to tumor biology.

Improved awareness of these atypical presentations is essential to avoid diagnostic and therapeutic errors, optimize patient management, and potentially improve outcomes in metastatic breast cancer with gynecologic involvement.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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