Endometrial metastasis of breast cancer: A Case Report and Review of the Literature

Abstract :

Endometrial metastasis of breast cancer is an exceptionally rare occurrence, with limited cases reported in the literature. While breast cancer commonly metastasizes to bones, lungs, liver, and brain, endometrial involvement remains unusual and diagnostically challenging. This case report describes a 48-year-old female with a significant family history of breast cancer, presenting with locally advanced left breast carcinoma and widespread metastases, including brain, bone, and endometrial involvement. Initial imaging and histopathology suggested a primary endometrial tumor, but immunohistochemical analysis confirmed metastatic breast carcinoma. This case highlights the diagnostic complexities of distinguishing primary endometrial malignancies from metastatic lesions, particularly in advanced breast cancer. The patient's aggressive disease progression, marked by complications such as lesional epilepsy and hydronephrosis, underscores the need for a multidisciplinary approach to diagnosis and management. This article reviews the literature on endometrial metastases of breast cancer, emphasizing diagnostic challenges, therapeutic implications, and prognostic considerations.

Keywords: Breast cancer, endometrial metastasis, immunohistochemistry .

1-Introduction

Metastatic breast cancer to the endometrium is an exceptionally rare phenomenon, with only a few cases reported in the literature. While breast cancer typically metastasizes to sites such as bones, lungs, liver, and brain, endometrial involvement remains uncommon and diagnostically challenging. The clinical presentation often mimics primary endometrial or cervical malignancies, necessitating a thorough histopathological and immunohistochemical (IHC) evaluation to confirm the diagnosis. This case report presents a patient with metastatic breast cancer involving the endometrium, illustrating the diagnostic complexities and therapeutic dilemmas associated with this condition. The integration of imaging, histopathology, and IHC is crucial for accurate diagnosis and management. By reviewing the literature, this article aims to enhance understanding of this rare entity, emphasizing the importance of a multidisciplinary approach to improve patient outcomes.

2-Case Presentation

Patient:

A 48-year-old single female patient, previously operated on for a uterine fibroid 12 years ago, presented with a significant family history of breast cancer:

- Sister currently undergoing treatment for breast cancer.
- Three first-degree cousins treated for breast cancer.
- Brother who passed away following a brain tumor.

History of Current illness:

The patient's symptoms began two months prior to consultation, marked by headaches and balance issues, prompting a brain scan.

Initial physical examination:

- **General Examination: WHO performance status 2; conjunctiva normally colored.**
- **Abdominal Examination: Soft abdomen, normal breathing, no signs of tumor syndrome (e.g., no hepatomegaly or splenomegaly).**
- **Clinical Breast Examination:**
    - **Left Breast: A mass involving the entire breast, hard in consistency, fixed, ulcerated, and fungating, centered in the peri- and retroareolar region. It oozes upon contact. A second hard mass adjacent to the first was noted in the axillary tail. Both masses were fixed to the deep tissue planes.**
    - **Right Breast: No abnormalities detected (RAS: *Rien à signaler*).**
    - **Lymph Node Areas: Multiple left-sided lymphadenopathies, including a fixed lymph node measuring approximately 3 cm in the largest diameter.**
    - **Clinical Staging: cT4dN2Mx.**

Imaging studies:

- **Brain Scan:** Revealed a lesion in the right cerebellar region measuring 36x32 mm, with a mass effect, and a second suspicious-looking lesion in the fronto-parietal area.
- **Brain MRI:** Lesions primarily suggestive of secondary brain metastases in the posterior fossa, temporal, and parietal regions.
- **CT Scan of the Chest, Abdomen, and Pelvis (CTAP):**

-Posterior Fossa Lesion: A tissue process involving the right cerebellar hemisphere, with irregular borders, significant contrast enhancement, and a central hypodense area suggestive of necrosis. It measures approximately 42x40 mm, causing a mass effect and compressing the fourth ventricle (V4).

-Left Breast Tumor: A large tumor mass involving all quadrants of the left breast, heterodense with spiculated borders, infiltrating the skin anteriorly (with skin thickening) and the pectoralis major muscle posteriorly. It measures 60x40 mm.

-Axillary Lymphadenopathy:** Infiltrating lymph nodes in the axillary region and axillary extension, encasing the left axillary artery over a 90° circumference. The largest node measures 26x27 mm in diameter.

-Internal and External Mammary Lymphadenopathy:** The largest node measures 8 mm in short axis.

-Subcutaneous Nodules:** A few permeation nodules in the internal mammary and subscapular regions on the left side.

-Bladder Lesion:A nodular growth at the vesico-ureteral junction measuring 15x11 mm, showing significant contrast enhancement. It causes right-sided hydronephrosis, with a renal pelvis measuring 18 mm.

-Uterus:The uterus is enlarged and heterogeneous, with hypertrophic changes in the cervico-isthmic region.

-Bone Lesion: An osteolytic lesion involving the right border of the D2 vertebra, suspicious in appearance.

Conclusion: Locally advanced left breast tumor with extension to the brain and bones. Suspicious nodule at the right vesico-ureteral junction causing ipsilateral hydronephrosis. Heterogeneous uterus with pathological endometrial thickening, requiring correlation with pelvic MRI findings.

Laboratory tests:

- Liver function tests and complete blood count were within normal limits.
- Serology for hepatitis B, hepatitis C, and human immunodeficiency virus were negative.
- Serum CA15.3 levels were elevated.

Histopathological analysis:

Macrobiopsy of the left breast lesion:

- Infiltrating ductal carcinoma, NOS type, Grade III (SBR):** Invading the skin.

-*Receptor status:

- ER (Estrogen Receptor): 100% positive.
- PR (Progesterone Receptor): 25% positive.
- HER2: Scored 3+ (positive).
- Ki-67: 65%.

Microbiopsy of the tissue mass at the junction of the inner quadrants (JQI) of the right breast:

- Findings consistent with subacute mastitis, with no evidence of tumor lesions.

Endometrial curettage biopsy:

- Poorly differentiated tumor process: The origin (endometrial or cervical) cannot be determined based on the biopsy.

Immunohistochemistry (IHC) of the endometrial biopsy:

- Poorly differentiated carcinomatous tumor proliferation:
    - GATA3: Positive.

- HER2: Positive.
- Hormone receptors (RH): Positive.

The IHC profile is similar to the previously diagnosed breast carcinoma, strongly suggesting that the endometrial lesion represents a metastasis from the breast carcinoma rather than a primary endometrial tumor.

BRCA1 mutation analysis: No abnormalities detected in exons 11 and 12.

BRCA2 mutation analysis: No mutation

Treatment and evolution:

The patient was started on Paclitaxel + Trastuzumab + Pertuzumab. After five cycles of treatment, the clinical course was marked by the occurrence of three episodes of right-sided hemibody seizures, with regaining of consciousness between episodes. The patient exhibited postictal mutism. Paradoxically, the brain MRI showed regression of some metastatic lesions and no new brain lesions. The diagnosis of lesional epilepsy secondary to brain metastases was made, and the patient was started on Depakine (valproate) + Urbanyl (clobazam).

One month after this episode, the patient developed anuria. An abdominopelvic CT scan revealed worsening of significant right-sided hydronephrosis, with the renal pelvis measuring 42 mm in AP diameter (compared to 32 mm previously), upstream of thickening of the right postero-lateral bladder wall invading the ureteral orifice. There was also an increase in the number and size of left-sided parietal permeation nodules.

The decision was made to investigate the bladder wall thickening through a cystoscopy with biopsy. However, the patient developed altered consciousness and subsequently passed away.

3-Discussion

Metastases to the female genital tract from extra-genital sites are rare, with the majority arising from malignancies of the gastrointestinal tract (37%) and breast (34%) (1) (2). Breast cancer can disseminate through direct extension, lymphatic pathways, and hematogenous spread. Although abnormal uterine bleeding is frequently the initial symptom of uterine metastases in women with a history of malignancy, as observed in our case, asymptomatic presentations have also been documented in the literature. (3)

Metastatic breast cancer involving the uterus frequently presents diagnostic challenges for both clinicians and pathologists. While the morphology of the tumor does not predict the timing or site of recurrence, recent studies indicate that infiltrating lobular and ductal carcinomas exhibit distinct patterns of metastasis (4) (5) .However, no significant differences in the distribution of metastases have been observed between classic infiltrating lobular carcinoma and its variants, including solid, alveolar, mixed, and signet ring patterns (6) (7).

The underlying reason for the distinct metastatic patterns between infiltrating lobular carcinoma (ILC) and infiltrating ductal carcinoma (IDC) remains unclear. It has been proposed that the loss of expression of the cell-to-cell adhesion molecule E-cadherin in ILC, which is typically retained in IDC, may contribute, at least in part, to the differing metastatic behavior of these tumor types (4) (8). Recent studies have demonstrated that invasive ductal and lobular carcinomas display distinct patterns of E-cadherin expression—whether membranous or cytoplasmic, normal or aberrant—both at the primary tumor site and in metastatic lesions. This suggests that E-cadherin may play differing roles in the biological behavior of each tumor type (9).
Limited studies have explored breast cancer metastases to the uterus. A case series published in 1982 identified 63 instances of uterine metastases originating from extra-genital sites, with breast malignancies accounting for 43% of these cases. The study revealed that when uterine metastases occur, the myometrium is more frequently involved (96%) compared to the endometrium (42%) (1). Distinguishing between a metastatic breast tumor and a primary genital neoplasm is crucial, as their treatment approaches and prognoses differ significantly , a primary uterine neoplasm can often be managed with surgical resection, whereas surgical intervention is generally not recommended for uterine metastases, with systemic chemotherapy likely being a more appropriate treatment option. (10).

However, according to Kaplan-Meier survival analysis, it remains unclear whether hysterectomy improves survival outcomes (11).On the other hand, due to the limited number of reported cases, there is insufficient data to fully understand the prognosis. While most studies have regarded uterine metastasis as a poor prognostic indicator, often associated with pre-terminal stages, further research is necessary to enhance our understanding of optimal treatment strategies and to establish a more accurate prognosis (12).

4-Conclusion

Endometrial metastasis of breast cancer is a rare and diagnostically challenging condition, as highlighted by this case report. The patient's presentation underscores the importance of immunohistochemistry in distinguishing metastatic breast cancer from primary endometrial malignancies. Despite aggressive systemic therapy, the disease's rapid progression and complications emphasize the poor prognosis associated with such advanced metastatic patterns. This case reinforces the need for a multidisciplinary approach to diagnosis and management. Further research is essential to better understand the biology of breast cancer metastasis to rare sites like the endometrium and to develop more effective treatment strategies for improved patient outcomes.

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