



Case Report

Her-2 Discordance Between Primer and Metastasis in Atypical Presentation of Metastatic Breast Cancer at the Time of Diagnosis: A Case Report

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Abstract

Breast cancer (BC) is the most common female cancer, the second most common cause of cancer death in women, and the main cause of death in women ages 40–59. The most common sites of BC metastases are liver, lung and bones. Metastases to the female genital tract from extragenital cancers are rare. Breasts and the gastrointestinal tract are the most common sites of the primary tumor. Several studies have carried out retrospective analyses comparing the ER, PR, and HER2 status of primary tumors and paired metastasis. We reported that HER2 discordance between primary and metastatic lesion in a 70-years old, postmenopausal woman who was diagnosed as invasive ductal carcinoma (IDC) with bone and endometrial metastases at the time of diagnosis.

Keywords: Breast cancer, Her2 discordance, metastasis

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Breast cancer (BC) is the most common female cancer, the second most common cause of cancer death in women, and the main cause of death in women ages 40–59.^[1] About 1–5% of the patients already show distant metastases at the time of diagnosis. The most common sites of BC metastases are liver, lung and bones.^[2–4] Metastatic carcinoma of the uterus usually originates from other genital sites, most commonly being from the ovaries.^[5, 6] In general, breast and gastrointestinal cancers are the most frequent extragenital tumours metastasising to the lower genital tract.^[7, 8]

Uterine metastasis of breast cancer has been previously reported to occur in 2–15% of patients, and invasive lobular carcinoma (ILC) is the most common histopathologic type

to metastasize to the uterus.^[9–12] If the uterus would be infiltrated, abnormal uterine bleeding is usually the most common manifestation.^[13] However, most of the uterine metastases are found on autopsy.^[14]

Estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) are the most important markers used in management of BC, for neoadjuvant, adjuvant and metastatic disease treatment. HER2 is amplified in approximately 20–25% of BC. HER2 amplification has been associated with tumor invasive, progressive regional and distant metastases, and poor prognosis in BC.^[15, 16] In routine clinical practice, management of patients with metastatic BC is frequently based on the biomarker characteristics of the primary

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tumor. However hormone receptors and HER2 status may change throughout tumor progression from primary tumor to the metastatic lesions. Several studies have suggested that there may be significant discordance of ER, PR, and HER2 status when comparing primary breast tumor with metastasis.^[17-21] Thus, biopsies of metastatic tissue should be taken as a routine procedure, and marker investigations at recurrence or metastatic carcinomas may potentially improve patient management and survival.^[22]

We reported that HER2 discordance between primary and metastatic lesion in a 70-years old, postmenopausal woman who was diagnosed as invasive ductal carcinoma (IDC) with bone and endometrial metastases at the time of diagnosis.

Case Report

A 70-years old woman with a postmenopausal period of 25 years presented to general surgery outpatient clinic with pain at left breast over one year which worsened within prior 3-4 months.

A spiculated nodule (3x2.5 cm in size) with a few microcalcified foci and BIRADS score of 5 at inner quadrant of left breast was detected on mammogram. Tru-cut biopsy was reported as invasive ductal carcinoma. Hormone receptors were as follows: ER, 90% (positive); PR, (negative) and HER2 (++). HER2 was (++) in immunohistochemical (IHC) staining. And than HER2 was re-evaluated with fluorescent in situ hybridization (FISH) method and HER2 amplification was negative.

Mediastinal lymph nodes and bone and uterus metastases were detected on Fluor-18-fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) imaging which was performed for staging (Figs. 1, 2). Accordingly, the patient was considered as primary metastatic malignant breast neoplasm.

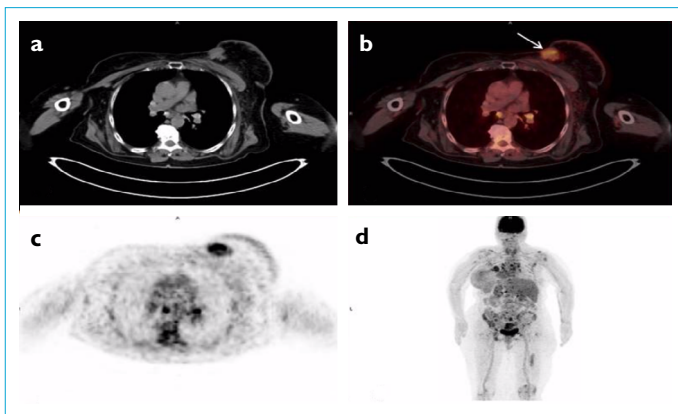


Figure 1 (a-d). Transaxial CT (a), fused (b), PET (c) and MIP (d) images of the 18F-FDG PET/CT scan. Primary tumor in the left breast is shown with arrow in the fused image.

CA 15-3 was found to be >300 IU/mL. Paclitaxel and zoledronic acid were prescribed to the patient. The endometrial sampling was reported as invasive breast carcinoma. Immunohistochemical staining showed in endometrial tissue sample: ER, 80% (positive), PR, 70% (positive) and Cerbb2, (+++). Trastuzumab was added to therapy (Figs. 3-7).

Discussion

Metastases to the female genital tract from extragenital cancers are rare. Breasts and the gastrointestinal tract are the most common sites of the primary tumor. Ovaries are most frequently affected by metastases accounting for

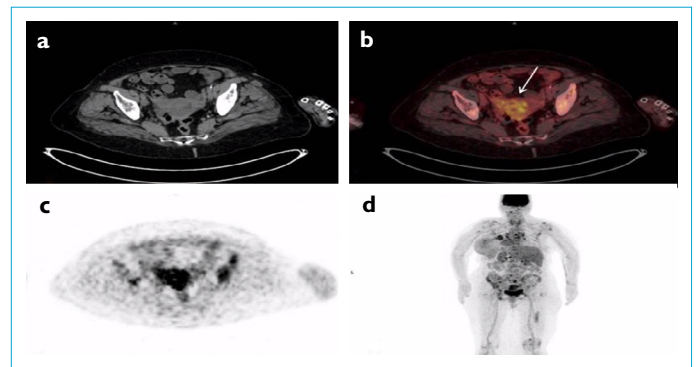


Figure 2 (a-d). Transaxial CT (a), fused (b), PET (c) and MIP (d) images of the 18F-FDG PET/CT scan. Uterine metastases were depicted on 18F-FDG PET/CT imaging (arrow, b).

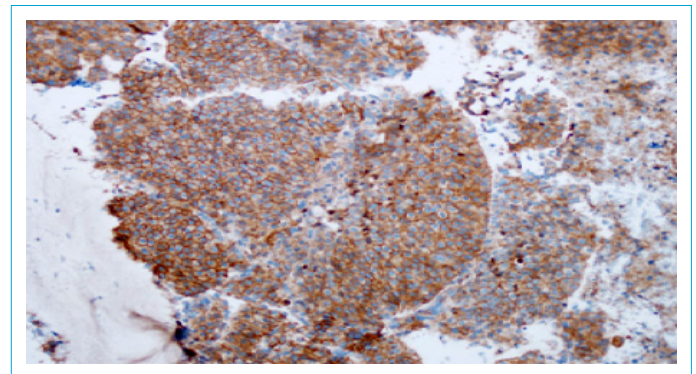


Figure 3. HER2 X20: Common Membranous and strong immunopositive.

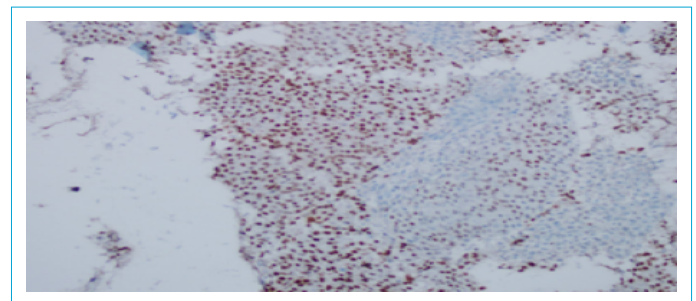


Figure 4. ER X20: nuclear and strong immunopositive.

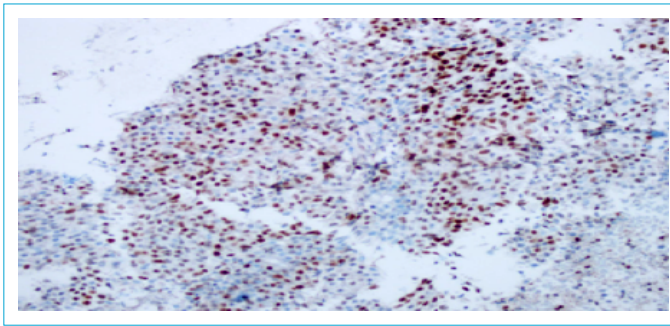


Figure 5. PR X20: Nuclear and strong immunopositive.

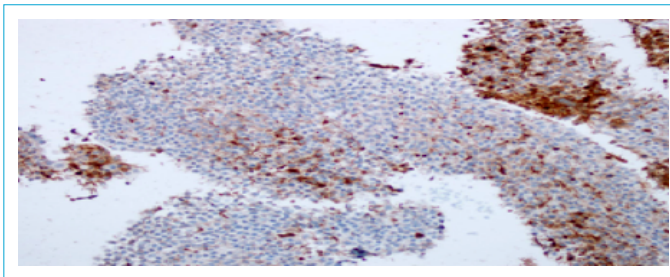


Figure 6. GCDFP-15 x20: focal and diffuse immunopositive.

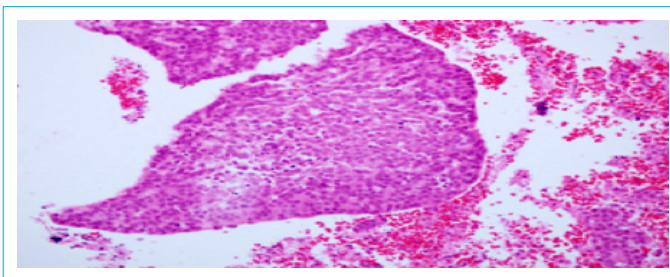


Figure 7. Hematoxylin eosin X20: Neoplasia forming the nodulation.

75.8%, followed by vagina (13.4%), uterine corpus (4.7%), cervix (3.4%), vulva (2%), and salpinx (0.7%).^[5] Uterine metastases usually occur secondary to local lymphatic spread from the ovarian involvement and thus isolated uterine metastases from the extragenital tumors are rare and probably hematogenous.^[23] It was demonstrated that involvement of the myometrium only accounts for 63.5%, followed by myometrium and endometrium (32.7%) and endometrium only (3.8%).^[6] Endometrial invasion, seen rarely, was detected in our case. Abnormal uterine bleeding is often the first symptom when the endometrium is involved. However, if the infiltration would affect myometrium only, patients may often be asymptomatic.^[13] In our case, there was no abnormal uterine bleeding despite endometrial invasion which was detected during asymptomatic period by using PET-CT scan.

ILC of the breast is responsible for more than 80% of metastases in gynecologic organs. The sites of metastatic spread in ILC differ from those of IDC. In ILC, the gastrointestinal tract,

peritoneum, retroperitoneum, and gynecologic organs have been reported as metastatic sites. In IDC the common metastatic sites are the lung, bones, liver, and brain.^[2-4, 7, 23] IDC accounts for approximately 70–75% of all BC compared to ILC that only accounts for 5–20%. Despite of its lower incidence in all BC, ILC is the most frequent histologic type that metastasizes to the female genital tract in more than 80% of all cases. Our patient is a rare case due to IDC.

Discordance of the HR or HER2 expression between the primary cancer and metastatic lesion is an important issue to select the optimal treatments for patients with metastatic breast cancer. Several studies have carried out retrospective analyses comparing the ER, PR, and HER2 status of primary tumors and paired metastasis.^[22] Nii-kura et al. performed a retrospective study to compare HER2 status between the primary tumor and metastatic sites in 182 patients with HER2-positive primary tumors. A discordance of 23.6% (43 patients) was found in patients with metastatic sites, where HER2 was positive in primary tumors and negative in metastatic tumors. Patients with discordant HER2 status had significantly shorter overall survival than patients with concordant HER2 status. This study indicates that some patients who have not received metastatic tumor biopsies might be receiving unnecessary treatment. The data strongly support the need for biopsies of metastatic lesions to accurately determine the patient prognosis and appropriate use of targeted therapy.^[24] In a retrospective study conducted by Liedtke et al. a total of 789 patients with recurrent breast cancer were studied. Discordance of ER, PR, and HER2 expression between primary and metastatic tumors was 18.4%, 40.3%, and 13.6%, respectively. Among discordant cases, the change from receptor-positive breast cancer to triple-negative status was 14.3%; only in 9.5% did triple-negative tumors change to a receptor-positive subtype.^[25] Lower et al.^[21] performed a retrospective study comparing HER2 expression between the primary and metastatic lesions in 382 patients, the discordance rate was 33.2%, the primary lesion was positive and the metastasis negative in 90 patients (23.6%), and the primary lesion was negative and the metastasis positive in 37 patients (9.7%). This study shows the significant discordance of HER2 expression between primary and metastatic tumors, and the determination of HER2 status in metastatic disease should be attempted.

In our patient, ER and PR was positive. HER2 was +2 positive in immunohistochemical staining. HER2 was re-evaluated with fluorescent in situ hybridization (FISH) method and HER2 amplification was negative in primary lesion. In metastatic endometrial biopsy ER and PR was positive.

HER2 was +3 positive in immunohistochemical staining. An apparent discordance was detected in HER2 receptor between primary BC and endometrial metastasis. This case was also presented due to rarity of uterine metastases in invasive ductal carcinoma. Gynecological physician should be aware of the possibility of primary metastatic breast cancer to the lower genital tract. Possibility of goal-directed therapy appeared due to HER2 positivity in re-evaluation of material obtained from invasion site in the patient. We can have chance to make changes in treatment strategies by re-evaluation of tumor tissue at metastasis site in patients with BC.

Disclosures

Informed Consent: Written informed consent was obtained from the patient for the publication of the case report and the accompanying images.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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