

Metastasis from endometrial carcinoma to bilateral breasts presenting as inflammatory breast lesions

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Summary

Background: Endometrial carcinoma rarely metastasizes to the bilateral breasts and presents as an inflammatory breast lesion. In this paper, we report a case of bilateral breast metastatic endometrial carcinoma and describe the clinical and pathological features. It is the second case of this kind of disease and the first case report with full clinical data. **Case report:** A 56-year-old Chinese woman (G3, P3) with endometrial carcinoma received cytoreductive surgery and chemotherapy. Approximately 22 months later, she presented with pain in the right axillary region and edema of the right breast. The pathology report confirmed multifocal invasive papillary adenocarcinoma of the right mammary gland, consistent with endometrial carcinoma metastasis. Although she received many lines of chemotherapy, the disease still progressed and metastasized to the contralateral breast. Gefitinib (Iressa) improved symptoms temporarily. **Conclusions:** Bilateral breasts metastasis of endometrial carcinoma is rare and difficult to treat. Molecular targeted therapy may be an effective treatment for breast metastasis.

Key words: Endometrial carcinoma; Metastasis; Breast cancer.

Introduction

Endometrial carcinoma is the fourth most common gynecologic cancer in the United States. The American Cancer Society estimated that 42,160 women were diagnosed with endometrial cancer and 7,780 died of their disease in 2009 [1]. Primary gynecologic malignancies rarely metastasize to the breast and account for about 0.17% of all cases of metastases to the breast [2]; furthermore, only 10% of those originate from endometrial carcinoma [3]. To the best of our knowledge, metastasis to the breast from an endometrial carcinoma has seldom been described in the literature. Metastases to the breast have distinct clinical, radiographic, and histological features and should be suspected in a patient with a breast mass and a known extramammary primary cancer.

Here, we report on a case of metastatic adenocarcinoma of endometrial cancer in the breast which presented as an inflammatory breast lesion.

Case Report

A 56-year-old Chinese woman (G3,P3) presented with vaginal bleeding accompanied by lower abdominal pain in June 2006. Menarche had occurred at the age of 13 years after normal breast and pubic hair development. The patient menstruated regularly until she reached menopause at the age of 50 years and had no history of oral contraceptive usage or exposure to exogenous hormones. There was no family history of malignancies.

Transabdominal ultrasonography revealed complex cystic structures in both ovaries measuring 5 cm x 4 cm, with an

overall increase in uterine volume. Fractional curettage of the uterus showed poorly differentiated adenocarcinoma of the uterus. Therefore, she received cytoreductive surgery and nine cycles of postoperative systemic chemotherapy with cyclophosphamide and cisplatin. During the procedure, metastatic disease of the stomach, liver and greater omentum was found. The pathology report (Figure 1A) described uterine papillary serous carcinoma (UPSC) with moderate differentiation at Stage IVB (according to the Federation of Gynecology and Obstetrics (FIGO) staging system).

Approximately 22 months after chemotherapy, the patient presented with edema of the right breast and pain in the right axillary region. Physical examination did not reveal any obvious breast mass. A chest computed tomography (CT) scan detected many nodules in the lungs, multiple enlarged lymph nodes in the right axillary region, a swollen breast, and thickened skin and muscles of the chest wall. Biopsy of the lymph nodes in the right axillary region showed metastatic adenocarcinoma (moderately differentiated). She was presumed to be suffering from a second primary breast cancer. After one cycle of chemotherapy with docetaxel and pharmorubicin, she received a right breast and right axillary region lymph node resection. However, pathology (Figure 1B) showed multifocal invasive papillary adenocarcinoma of the right mammary gland consistent with endometrial carcinoma metastasis. The pathology specimen was negative for estrogen receptor, progesterone receptor, Her-2/neu, CA-153 and carcino-embryonic antigen.

After three cycles of chemotherapy with docetaxel and cisplatin, her right upper extremity swelled progressively, accompanied by limitation of movement, soreness, prostration and multiple blisters on the skin of the right axilla and right anterior part of chest. She then received two cycles of chemotherapy with pemetrexed and pharmorubicin. Unfortunately, the right upper extremity symptoms still progressed. Oral etoposide did not improve symptoms and neither did a later single cycle of palliative chemotherapy with gemcitabine and cisplatin (Figure 1C, D).

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Figure 1. — A) Serous adenocarcinoma of the endometrium - FIGO grade 2 (black arrow); B) Right breast with metastatic serous adenocarcinoma (black arrow). Both, hematoxylin and eosin stain, 200 \times ; C) Edema of the right upper limb; the skin was purple with decreased flexibility; D) Edema of the right shoulder, blisters, skin ulceration, palpable 3 cm \times 3 cm size under the nodule; right breast resection.

After that, targeted therapy with gefitinib, an epithelial growth factor receptor (EGFR) inhibitor, was administered at 250 mg per os daily for 20 days. The edema and soreness of her right upper extremity were significantly relieved after five days of treatment, although the improvement lasted only five days. One month later, the patient developed a metastasis to the contralateral breast and the skin of the chest wall. The metastatic infiltration presented as diffuse thickening of the skin and increased density of the breast, resembling inflammatory disease or damage after radiotherapy (Figure 1E). Mammograms demonstrated that dense glandular tissue occupied almost the entire breast (Figure 1F). Because of extreme exhaustion, she could not tolerate further chemotherapy or radiotherapy and she was directed to receive supportive care. Finally, she was unable to overcome the aggressive metastatic course of the

primary tumor and expired 3.5 years after her initial diagnosis. All these treatments obviously prolonged her survival.

Discussion

Women with metastatic endometrial cancer have an overall poor prognosis, with estimated survival of less than one year. The breast is an unusual site for metastatic disease. Between 0.5% and 2% of the breast tumors have been identified as originating from metastatic deposits elsewhere [4]. The most common origin of metastasis to the breast is contralateral primary breast carcinoma. Therefore, the Medline database was searched in order to find relevant published reports from

Fig. 1e



Fig. 1f

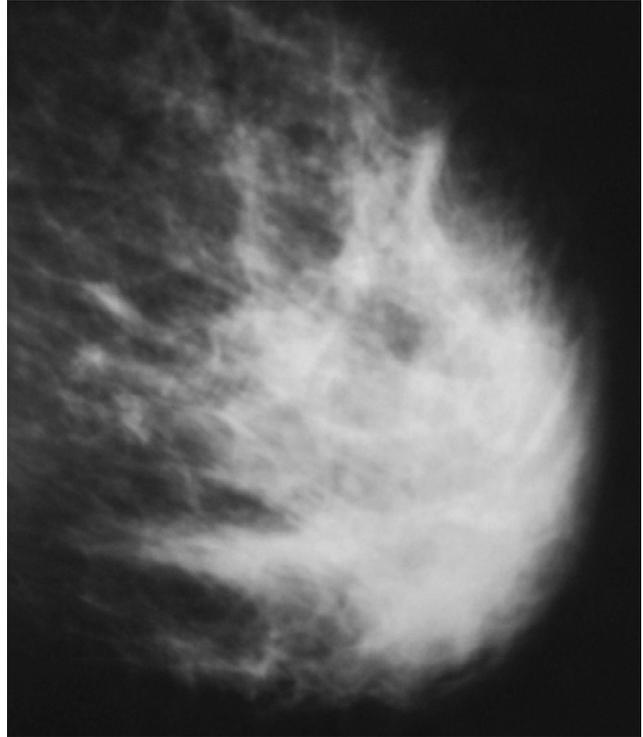


Figure 1. — E) Diffuse thickening of the skin and increased density of the left breast, accompanied by decreased skin elasticity. There were multiple nodules in the skin of left axillary and left breast; F) Mammograms of the left breast demonstrated that dense glandular tissue occupied almost the entire breast tissue.

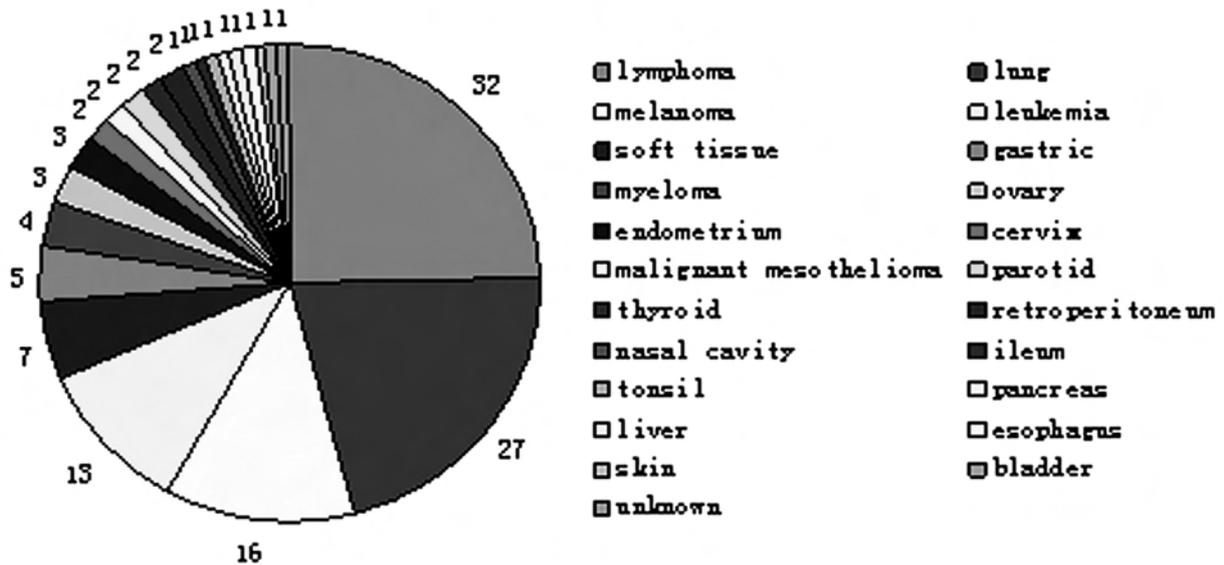


Figure 2. — Origin of metastasis to the breast in 135 patients.

January 1969 to December 2005 so as to analyze the origin of the metastatic disease to the breast [5-10]. These findings are summarized in Figure 2. The five most common extramammary malignancies which metastasized to the breasts were identified as lymphoma, bronchogenic carcinoma, malignant melanoma, leukemia, and soft tissue malignancies. These data are partially in agreement with those published by O'Donnell *et al.* [11].

Metastasis of UPSC to the breast is an extremely rare

event with only one case reported in the English literature since initially described [5]. Here, we have reported the second case and it is the first case report with full clinical data.

Treatment options for advanced stage endometrial cancer include the use of surgery, chemotherapy, radiotherapy, targeted therapy, or a combination [12]. A retrospective multi-institutional study of cytoreductive surgery for Stage III/IV UPSC showed a trend toward survival

benefit in women who were optimally cytoreduced compared with women who had bulky residual disease, a finding that needs to be confirmed by prospective studies [13]. The chemotherapy approach has focused largely on platinum-based combinations. Most studies investigating the treatment for advanced-stage disease indicate that chemotherapy is the preferred modality of treatment [14]. Whole abdominal radiotherapy vs doxorubicin and cisplatin in women with advanced endometrial carcinoma has been investigated in a Gynecologic Oncology Group (GOG) trial which concluded that chemotherapy was superior [15]. A multi-center retrospective analysis of patients with surgical Stages III and IV endometrial cancer indicated that chemotherapy followed by radiation and then further chemotherapy was associated with improved survival for both overall survival and progression-free survival in women with advanced stage disease [16].

A better understanding of the molecular genetic mechanisms of non-endometrioid endometrial cancer has led to the development of targeted therapies that inhibit angiogenesis and malignant cell growth and proliferation [17]. Several of these targeted agents are currently being investigated in endometrial carcinoma [18]. Chemotherapy is the preferred treatment modality in most cases of advanced-stage endometrial cancer. However, our patient was resistant to many effective chemotherapy drugs and the disease progressed. We therefore tried gefitinib, indicated for the treatment of certain types of metastatic cancer. In contrast to chemotherapy, gefitinib significantly improved symptoms. However, the curative effect was still unsatisfactory. Further studies are needed to illustrate the key signal transduction pathway in endometrial carcinogenesis, which may help identify effective biological targets suitable for tailored therapies.

Metastatic endometrial carcinoma to the bilateral breasts is extremely rare and might appear within two years after the diagnosis of primary tumor. This possibility should be considered when an unusual biomorphic pattern appears in a tumor. As with other distant metastases of endometrial carcinoma, mammary gland involvement is associated with difficult management strategies and poor prognosis. Molecular targeted therapy may represent a promising option for this kind of cases [19].

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