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Case Report

Recurrent Malignant Phyllodes Tumor of Breast with Gastric Metastasis

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Abstract

Malignant phyllodes tumor of the breast (MPTB) is a rare breast malignancy. Surgery is the primary treatment for this malignant tumor. Adjuvant radiotherapy should be considered if the surgical margin is positive. The lungs and bone are the most frequent metastatic sites of MPTB; however, gastric involvement is rare. Herein, we report a 64-year-old woman with MPTB. Surgery was the initial treatment; however, lung and gastric metastases were found 5 years later. Palliative chemotherapy with the CyVADIC regimen (cyclophosphamide, vincristine, doxorubicin, and dacarbazine) achieved a partial response. In conclusion, systemic chemotherapy can be one of the treatment options for patients with metastatic MPTB.

Keywords: Chemotherapy, malignant phyllodes tumor of the breast, metastasis

Introduction

Phyllodes tumor of the breast is a rare breast disease. It can be classified into benign, borderline, or malignant tumors according to the histological criteria. Curative surgery is the main treatment for a malignant phyllodes tumor of the breast (MPTB). Radiotherapy should be considered for patients whose surgical margin is positive or in whom the tumor size is more than 10 cm. Distant metastasis is not uncommon for patients with high-risk factors. The lungs, bone, limbs, and liver are the major metastatic sites;[1] however, metastasis to the gastrointestinal tract is rarely seen in MPTB patients. Palliative chemotherapy can be considered in patients with metastatic MPTB; however, the response rate is difficult to predict. Herein, we report a 64-year-old woman with MPTB with metastases in the lungs and stomach 5 years after the curative surgery.

Case Report

This 64-year-old woman was diagnosed with MPTB in July 2012 with the initial presentation of progressive enlargement of a left breast mass for 2 months. She received simple mastectomy without lymph node dissection. The pathologic report of the tumor showed stromal overgrowth and marked stromal cellularity. The mitotic activity was more than 10/10 in a high-power field [Figure 1, left], and

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immunohistochemistry (IHC) staining showed negative results for AE1/AE3, CD117, CD34, DOG-1, LCA, CD43, S-100 protein, desmin, and GATA3. The surgical margin was positive; however, she refused further adjuvant radiotherapy because of an unknown personal reason and she was then lost to follow-up. In January 2018, she came back to our emergency department because of anemia with syncope, off-and-on fever, and shortness of breath. She also complained of intermittent abdominal pain for 1 month and tarry stool passage for 1 week. A chest X-ray showed one ground-glass opacity over the right lower lung field [Figure 2a]. Chest computed tomography also showed a 5.8-cm tumor over the right lower lung field with mediastinal and subcarinal lymph node enlargement [Figure 3a]. Esophagogastroduodenoscopy was also performed for the tarry stool, which revealed a huge ulcerative tumor over the gastric body and angularis [Figure 4]. The pathologic report of the gastric ulcerative tumor showed a malignant pleomorphic spindle cell tumor with marked cellular pleomorphism [Figure 1, right]. IHC staining of the gastric lesion also showed all negative results, which was compatible with metastasis of previous MPTB. Under the impression of recurrent MPTB with lung and gastric metastases, she received systemic chemotherapy with the CyVADIC regimen (cyclophosphamide – 500 mg/m^2 on day 1, vincristine – 1.5 mg/m^2 on day 1, doxorubicin – 50 mg/m^2 on day 1, and dacarbazine – 250 mg/m^2 from day 1 to day 5; repeated every 3 weeks) in February 2018. Her fever subsided and no further gastrointestinal bleeding was noted after the first cycle of CyVADIC chemotherapy. Her hemoglobin level was stable through the treatment, except for occasional anemia during cytopenic status after chemotherapy. A partial response was further proved by chest computed tomography and X-ray after three courses of CyVADIC chemotherapy [Figures 2b and 3b]. She is currently still receiving CyVADIC chemotherapy.

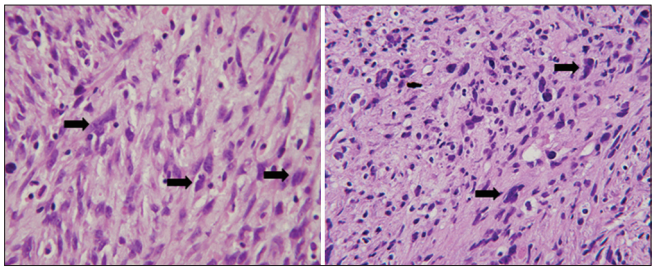

Figure 1: The two specimens (left: breast lesion in 2012; right: stomach lesion in 2018) showed identical features, including mixed epithelial and stromal proliferation, increased cellularity and mitotic counts (arrow)

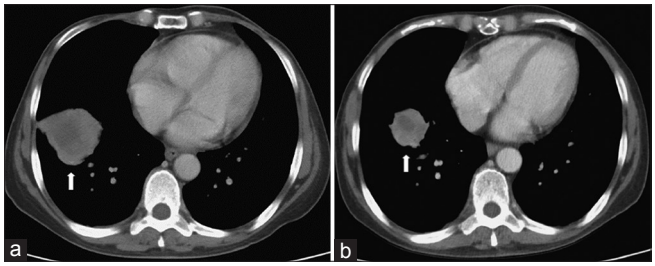

Figure 3: (a) Chest computed tomography in January 2018, before treatment, showed a tumor in the right lower lung of about 5.8 cm (arrow). (b) Chest computed tomography in May 2018, after three courses of chemotherapy, showed a great decrease in the size of the tumor (arrow)

Discussion

Phyllodes tumor of the breast is a rare breast disease. It is a fibroepithelial tumor characterized by a double-layered epithelial component arranged in clefts, surrounded by an overgrowing mesenchymal leaf-like component. The pathologic grading among benign, borderline, and malignant tumors depends on the histological criteria according to the World Health Organization proposed in 2003.[2] Most phyllodes tumors of the breast are benign (50%–60% of cases),[2,3] and only <1% of phyllodes tumors of the breast are malignant. The Surveillance, Epidemiology, and End Results study reported an average annual incidence of MPTB of 2.1 cases per million people.[1,4] Predominantly infiltrating margins, very high stromal cellularity of at least ten mitoses per ten high-power fields, and severe cellular atypia are the pathologic features of MPTB [Table 1].[5,6]

The diagnosis of MPTB is challenging. The median age at a diagnosis of MPTB is around 40–50 years. A unilateral, painless, palpable breast mass is the most common presentation.[5,7]

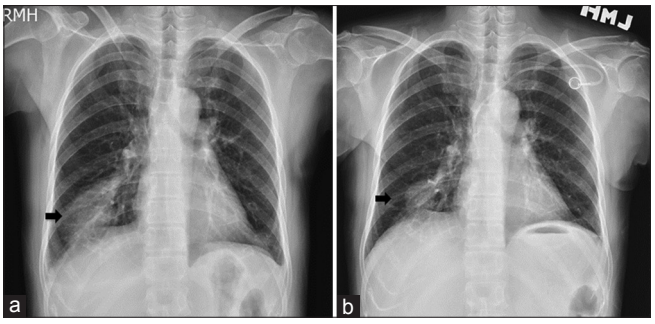

Figure 2: (a) Chest X-ray in January 2018, before the treatment, showed ground-glass opacity over the right lower lung (arrow). (b) Chest X-ray in May 2018, after three courses of chemotherapy, showed a decreased size of the lesion (arrow)

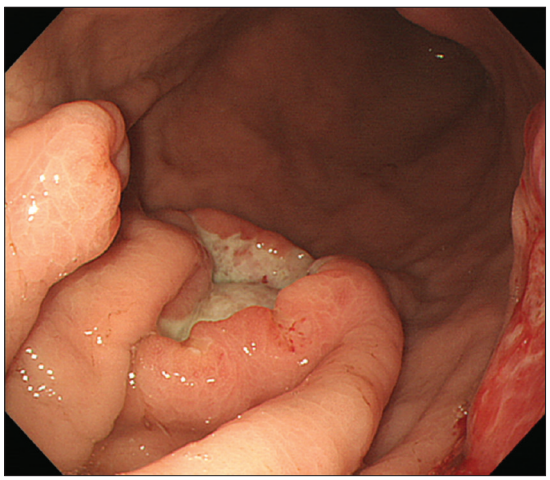

Figure 4: Esophagogastroduodenoscopy showed a huge ulcerative tumor over the gastric body and angularis

Table 1: Histologic features for the classification of a phyllodes tumor of the breast

Histologic feature	Benign	Borderline	Malignant
Mitotic activity	<4/10 HPF	4-9/10 HPF	≥10/10 HPF
Stromal cellular atypia	Mild	Moderate	Severe
Stromal overgrowth	Mild	Moderate	Severe
Tumor margins	Clear	Clear or infiltration	Infiltration

HPF: High-power field

Imaging studies such as mammography, breast MRI, and sonography have limitations to distinguish a fibroadenoma from a MPTB. Fine needle or core needle biopsy may also result in a misdiagnosis between these two types of tumors. Total resection of the tumor seems to be the only way to provide a definite diagnosis of MPTB.[5,8]

In terms of the initial treatment, breast conservative survey or mastectomy are the major treatments for MPTB.[1,3] Routine axillary lymph node dissection is not recommended, except when the possibility of lymph node involvement is identified. The incidence of lymph node involvement, however, is only <1%.[4,9] A clear resection margin has been confirmed to be the key factor for local recurrence and distant metastasis.[7] Although an appropriate width margin is still under debate, a free margin more than 1 cm is the consensus.[1,4,10] Therefore, breast conservative survey could be the treatment of choice if a free tumor margin can be achieved. Mastectomy is reserved for patients whose tumor-free margin cannot be obtained. Further adjuvant treatment after complete resection is controversial. According to some studies, adjuvant radiotherapy is only suggested for patients with a positive margin after mastectomy, those with a free margin <1 cm, or those with an initial lesion more than 10 cm in size.[1,11] Other prognostic factors such as age, degree of tumor necrosis, tumor size, increased stromal cellularity, stromal overgrowth, stromal atypia, increased mitotic activity, and cellular pleomorphism have been discussed in different studies.[5-7,10,12]

Local recurrence and distant metastasis are challenging issues with phyllodes tumors of the breast. Benign and borderline phyllodes tumors of the breast have a similar likelihood of local recurrence, accounting for 15% of cases; however, the local recurrence rate is twice as high in MPTB.[7,8,10] A clinicopathological analysis of 65 cases by Karim *et al*.[13] showed that Asian patients had a higher recurrence rate than non-Asian patients. The frequencies of distant metastasis in benign, borderline, and malignant phyllodes tumors of the breast have been reported to be 0%–2%, 3%–11%, and 6%–47%, respectively.[7,8,14] The majority of cases of metastasis occur within the first 3 years after the surgery. The lungs, bone, limbs, and liver are the most common metastatic sites;[1,9,12,14] however, abdominal visceral organ involvement, as seen in our patient, is rare.[9] Metastatic MPTB has a poor prognosis with a median survival from the diagnosis of metastasis of only 5–7 months.[14]

Surgery, radiotherapy, and systemic chemotherapy can be considered for patients with relapsed MPTB. Although the epithelial component of most phyllodes tumors of the breast contains estrogen and progesterone receptors, hormone therapy has not shown significant efficacy.[12,14] Palliative surgery and radiotherapy are reserved for individual or localized lesions. For distant metastasis, chemotherapy containing doxorubicin, ifosfamide, etoposide, dacarbazine, or cisplatin may be the best choice according to the past literature reviews and limited care reports.[9,14] According to the NCCN guideline, treatment followed by the suggestion of soft-tissue sarcoma is recommended.

Conclusion

MPTB is a rare malignant breast malignancy. Surgery with an adequate surgical margin is the primary treatment goal. Adjuvant radiotherapy has some role; however, the definite indication is not clear. MPTB rarely metastasizes to the visceral organs, and systemic chemotherapy may provide some benefits for patients with metastatic MPTB.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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