Metastatic gastric carcinoma to the breast: A case report and review of the Chinese literature

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Abstract. Breast metastasis is extremely unusual in gastric cancer patients worldwide. We herein report the case of a 39-year-old female Chinese patient presenting with symptoms of inflammation in the left breast. A biopsy did not reveal any evidence of malignancy. A modified radical mastectomy was performed and the postoperative pathological examination revealed infiltration by signet ring cell gastric carcinoma. A review of the Chinese literature was performed, and a total of 16 patients with breast metastasis from gastric carcinoma have been reported from 1990 onwards. This condition is associated with a poor prognosis, with a survival time of 1 month to 4 years. More studies are required to determine the optimal treatment.

Introduction

Gastric carcinoma is a common type of cancer in humans. However, metastasis of signet ring cell gastric carcinoma to the breast is extremely rare, with only ~40 cases reported according to the PubMed database (1,2) and only 16 cases reported in the Chinese literature to date. The incidence of metastasis to the breast is ~0.2-1.3% (3), with ovarian cancer being the most common primary site. Systemic therapy is recommended for metastatic breast cancer patients and the survival time is often <1 year (4). Correct diagnosis of primary or metastatic malignant tumor of the breast is extremely important for proper treatment. We herein report the case of a 39-year-old Chinese female patient with metastasis to the breast from signet ring cell gastric carcinoma and perform a review of the relevant literature.

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Case report

A 39-year-old female patient presented to the Shanghai General Hospital (Shanghai, China) in March, 2016, complaining of painful swelling of the left breast for 1 week. Physical examination revealed inverted nipple and pitted skin (peau d'orange sign) in the left breast (Fig. 1). A 2x1-cm mass with indistinct borders was identified below the left nipple and several non-fused enlarged lymph nodes were palpated in the ipsilateral axilla. The medical history of the patient included radical resection for poorly differentiated adenocarcinoma of the stomach 18 months prior. Postoperatively, the patient received 6 cycles of chemotherapy treatment as follows: The first course included cisplatin (dose unknown, day 1) + S-1 (40 mg, bid on days 1 and 14); courses 2-6 included oxaliplatin (150 mg, day 1) + S-1 (40 mg, bid on days 1 and 14). Over the last month, the patient underwent radical resection for ovarian metastasis from signet ring cell gastric carcinoma. The patient's father also had a history of gastric cancer.

The ultrasound examination revealed a solid heterogeneous mass in the left breast, suspected to be a malignant tumor, with edema and thickening of the subcutaneous soft tissue of the areola of the left breast (Fig. 2). In addition, two enlarged lymph nodes were palpated in the ipsilateral axilla. Ultrasound angiography revealed a slightly lower enhancement deeper in the left nipple (Fig. 3). A mammogram revealed heterogeneous architectural distortion and increasing uneven density in the left breast (Fig. 4). Enhanced magnetic resonance imaging revealed heterogeneous architectural distortion and skin thickening (Breast Imaging Reporting and Data System type 4) (Fig. 5). A chest computed tomography (CT) confirmed that the epidermis of the left breast was edematous and thickened and several small lymph nodes were detected in the left axilla (Fig. 6). A positron emission tomography/CT raised the suspicion of inflammatory breast cancer and bone metastasis.

Core needle biopsy of the left breast revealed ductal epithelial hyperplasia and infiltration by inflammatory cells, without any evidence of malignancy. The patient received treatment with azithromycin for 6 days. However, the inflammation was not controlled. The patient then underwent modified radical mastectomy. An intraoperative biopsy revealed ductal epithelial hyperplasia without a definitive diagnosis of malignancy. Finally, the postoperative pathological examination revealed signet ring cell carcinoma and metastasis was identified in all 23 retrieved axillary lymph nodes. Immunohistochemical

Figure 1. Left breast showing inverted nipple and pitted skin (peau d'orange sign).

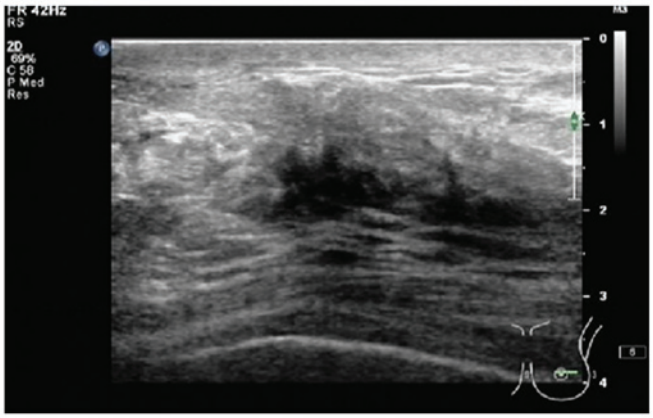

Figure 2. Ultrasonography of the breast revealing a solid heterogeneous mass in the breast, suspected to be a malignant tumor, with edema and thickening of the subcutaneous soft tissue on the left areola.

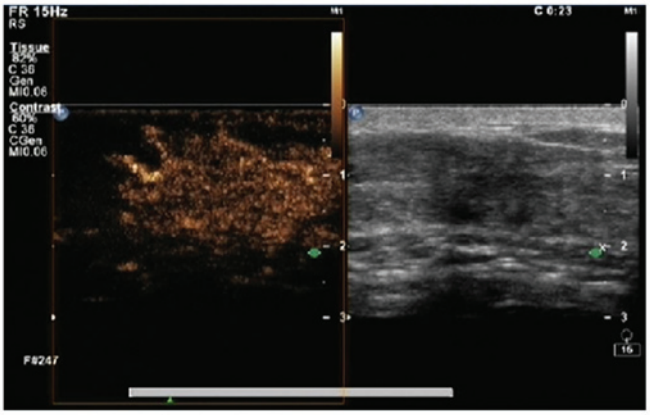

Figure 3. Ultrasound angiography of the left breast showing a slightly lower mass enhancement deep in the left nipple (left panel, contrast-enhanced tumor; right panel, appearance of the mass on B-ultrasound).

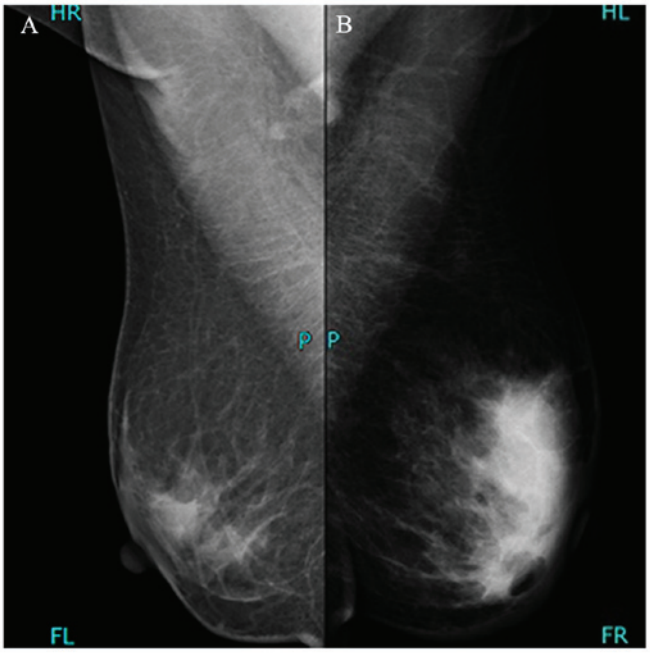

Figure 4. Mammogram revealing heterogeneous architectural distortion and increasing uneven density, with changes of the nipple and skin in the left breast (A) Right breast, normal breast tissue. (B) Left breast exhibiting an inverted nipple (arrow a) and heterogeneous architectural distortion with increasing uneven density (arrow b).

evaluation of the tumor revealed the following: Cytokeratin (CK)7$^-$, CK20$^-$, villin$^+$, carcinoembryonic antigen$^+$, caudal type homeobox transcription factor 2$^+$, CAM5.2$^+$, Ki-67 (50%), P53$^+$ and CerbB-2$^-$.

The patient received chemotherapy for gastric carcinoma with docetaxel (110 mg on day 1) and capecitabine (1.5 g, bid on days 1 and 14) but succumbed to the disease 3 months later. Written informed consent was obtained from the patient and her family regarding the publication of the case details and associated images.

Discussion

Breast metastasis from gastric carcinoma is extremely rare in clinical practice. Previous studies reported that only <0.3% of gastric cancer patients develop breast metastasis, which is far less frequent compared with liver metastasis (4-14%), the most common site of distant metastasis from gastric cancer (5,6). Only 16 cases have been reported in China thus far and are summarized in Table I (7-19). Of those 16 patients, 12 were diagnosed with signet ring cell carcinoma and 5 had multiple metastases.

In China, the age at diagnosis of patients with breast metastasis from gastric carcinoma ranges from 26 to 62 years (mean, 40.2 years; median, 38 years). In the international literature (20), the age of the patients developing breast metastasis from gastric carcinoma ranges from 22 to 70 years (mean, 45.5 years; median, 46 years). Due to the occult nature of gastric carcinoma, breast metastasis was the first manifestation of the disease in 43.8% (7/16) of the Chinese patients.

Table I. Patients with breast metastasis from gastric carcinoma in China.

Case no.	First author, year	Age, years	Histology	Clinical presentation	Breast operation	Interval	Other metastatic sites	Survival	(Refs.)
1	Lin, 1990	34	Signet ring cell	Mass	Mastectomy	4 months	-	Not stated	(5)
2	Zhu, 1994	51	Signet ring cell	Mass	Lumpectomy	[a]	-	Not stated	(6)
3	Li, 2001	42	Signet ring cell	Mass	Mastectomy	4 years	Ovary	4 years, died	(7)
4	Wei, 2004	62	Signet ring cell	Mass	Mastectomy	[a]	-	6 months, died	(8)
5	Zheng, 2005	52	Adenocarcinoma	Mass	Mastectomy	40 days	-	4 months, died	(9)
6	Wang, 2007	32	Signet ring cell	Mass	Lumpectomy	11 months	Ovary	19 months, died	(10)
7	Ye, 2007	26	Signet ring cell	Mass	Mastectomy	5 years	-	Not stated	(11)
8	Wang, 2011	41	Signet ring cell	Mass	Mastectomy	4 years	Colon	Not stated	(12)
9	Weng, 2011	34	Adenocarcinoma	Mass	None	[a]	-	Not stated	(13)
10	Tang, 2012	35	Adenocarcinoma	Mass	Lumpectomy	[a]	-	3 months, died	(14)
11	Hong, 2013	44	Signet ring cell	Inflammatory symptoms	None	3 years	-	1 month, died	(15)
12	Zhu, 2013	35	Adenocarcinoma	Mass	Mastectomy	[a]	-	3 months, died	(16)
13	He, 2015	48	Signet ring cell	Mass	None	[a]	-	Not stated	(1)
14	Tian, 2016	37	Signet ring cell	Mass	Mastectomy	4 years	Colon	18 months, died	(17)
15	Tian, 2016	31	Signet ring cell	Mass	Mastectomy	[a]	-	10 months, died	(17)
16	Yan, 2016	39	Signet ring cell	Inflammatory symptoms	Mastectomy	18 months	Ovary, bone	3 months, died	Present case

[a]Breast metastasis was the first manifestation of the disease.

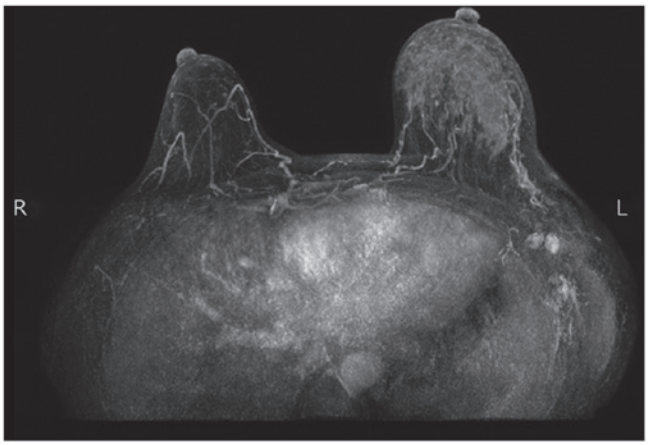

Figure 5. Enhanced magnetic resonance imaging suggesting inflammation or inflammatory breast cancer due to the heterogeneous architectural distortion and skin thickening (Breast Imaging Reporting and Data System type 4).

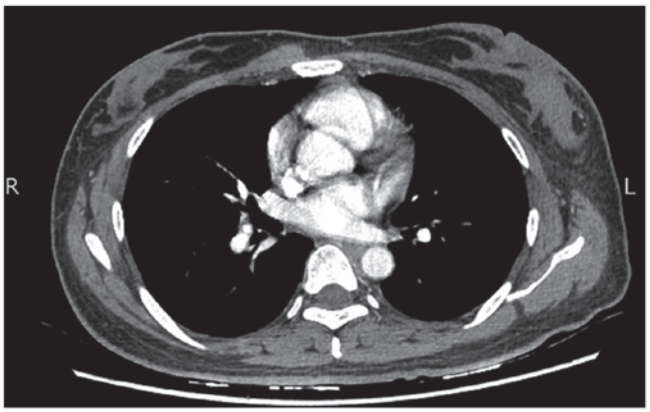

Figure 6. Chest computed tomography confirming swelling and thickening of the epidermis of the left breast. A number of small lymph nodes were identified in the left axilla.

Breast metastasis from gastric carcinoma generally presents as a mass or inflammatory symptoms. The majority (14/16) of the Chinese patients presented with a painless mass in the breast. To the best of our knowledge, our patient is the second reported case in China presenting with symptoms of primary inflammatory breast cancer, which is characterized by erythema and thickening of the skin with pitted skin (peau d'orange sign). The first case was reported in 2013 and only 11 cases of inflammatory breast metastases from gastric cancer have been reported thus far (4).

The treatment for breast metastasis from gastric carcinoma remains controversial. The majority (10/16) of the Chinese patients with breast metastasis from gastric carcinoma underwent modified radical mastectomy, 4 patients received a lumpectomy, and 2 patients only underwent biopsy. Lumpectomy is the current recommendation for the treatment of such patients (19). Qureshi *et al* (21) reported that radiotherapy is not effective in treating breast metastases, as it cannot prolong patient survival time. Additional investigation is required to determine the optimal treatment. All the patients received chemotherapy for the treatment of primary gastric carcinoma.

The prognosis of breast metastasis from gastric carcinoma is generally poor. The time from surgical treatment of gastric cancer to the diagnosis of breast metastasis varies from 40 days to 60 months in China, whereas 40 days to 72 months was reported by Iesato *et al* (20). The survival time of Chinese patients with breast metastasis varies from 1 to 48 months. He *et al* (1) retrieved 38 cases from the international literature and found an overall survival time of 12 days to 18 months. Hadju and Urban (22) reported that >80% of patients with breast metastasis from gastric carcinoma succumbed to the disease within 1 year.

As breast metastasis from gastric carcinoma is rare, increased awareness is necessary and this possible diagnosis should be considered when patients with a history of gastric cancer detect a new breast mass.

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