

Case Report

Breast metastasis of primary colorectal cancer: a case report

Shun Zhang, Tao Du, Xiaohua Jiang, Chun Song

Gastrointestinal Surgery, Shanghai East Hospital, Tongji University School of Medicine, Shanghai, P. R. China

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Abstract: Breast metastasis can mimic a primary breast cancer and may present confusing diagnostic problems. Its management differs from that of primary breast cancer, as illustrated by this case of a colonic metastasis to the breast. An 80-year-old woman whose breast tumor showed features of adenocarcinoma received wide excision. After one month, the patient presented with abdominal pain. In evaluation colon cancer was diagnosed. Considering endoscopy indicated stenosis of the sigmoid that would lead to obstruction of colon, laparoscopy-assisted sigmoidectomy was done. We searched Pubmed up to April, 2016. Metastasis to the breast from colorectal carcinoma is very rare and only 32 such cases have been reported in the literature. Most patients were female, the median age was 51.1 years, and the majority of metastases (48%) were to the left breast. In 5 cases the patients died an average of 14.5 months after the diagnosis of breast metastasis. Colorectal carcinoma metastatic to the breast is indicative of widely disseminated disease and a poor prognosis. It is important to make this distinction between primary breast cancer and a metastatic process, in order to provide the most effective and appropriate treatment for the patient and to avoid any harmful or unnecessary surgical procedures.

Keywords: Colorectal cancer, breast, metastasis

Introduction

Colorectal cancer is the third most common cancer in the world and second most common cause of cancer mortality after lung cancer. Distant metastasis is the most common cause of death in colorectal cancer patients and these sites often occur in the liver, lungs, peritoneal cavity and bone in descending order [1].

Breast metastasis can mimic a primary breast cancer and may present confusing diagnostic problems. The most common tumor that metastasizes to the breast is a contralateral breast carcinoma, followed by metastasis from hematopoietic neoplasms, malignant melanoma, lymphoma, sarcoma, lung, prostate, ovary, kidney, stomach, and carcinoid tumors [2].

The occurrence of breast metastases from extra mammary sites is rare [3]. In this paper, the case of an 80 year-old woman with colorectal carcinoma developing into breast metastasis is described.

Case report

In April 2015, an 80 years old female patient presented to local oncology hospital with a lump in her right breast discovered incidentally 3 days ago. She had no previous breast problems or family history of breast cancer. On physical examination, a 1.5 cm firm lump with no pain or nipple discharge was noted in the upper outer quadrant of her right breast. No lymph nodes were palpable. The ultrasound examination demonstrated a 9*11 mm hypoechoic solid lesion with no lymph nodes seen in the right axilla (BI-RADS 4). There was not internal but peripheral vascularity on color Doppler imaging. A mammogram showed a partially well-defined nodule without microcalcifications and axillary lymphadenopathy which was indeterminate but suspicious for neoplasm (BI-RADS 4). A contrast enhanced breast MRI examination demonstrated 1.5*1.8 cm sized irregular shaped enhancing mass in the upper outer quadrant of the right breast (BI-RADS 4C) (**Figure 1**).

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Figure 1. Mammographic image of the breast.

The patient was sent for an ultrasound guided core biopsy of the lesion. Histopathologic examination of the core biopsy samples revealed invasive adenocarcinoma. But she didn't only receive abdominal CT scan and gastrointestinal endoscopy but also the serum tumor markers test. Wide excision of the tumor and sentinel lymph node biopsy was performed. On histopathological examination, the tumor cells in the breast mass were compatible with the features of adenocarcinoma of gastrointestinal tumor origin. The harvested sentinel lymph node did not contain tumor cells. Immunohistochemical study revealed the following results: tumor cells were negative for ER, PR, Her2 and GCDFFP-15. The surgeon asked the patient to do a further gastrointestinal examination but the patient refused and was discharged.

In June 2015, nearly one month after his discharge, the patient presented to our emergency room because of a one-week history of alteration in her bowel habits, abdominal pain and distension, and nausea/that had aggravated in the previous 1 day. On physical examination, the abdomen was distended and bowel sounds were present. A detailed review of previous medical records was carried out and revealed the breast operation. There was no family history of any bowel cancers. Laboratory tests showed serum carcinoembryonic antigen (CEA) level elevated to 199.300 ng/mL (normal, 0 to about 6.9 kU/L), serum carbohydrate antigen (CA) 125 level elevated to 57.820 U/mL (normal, 0 to about 35.0 kU/L), and serum CA199 level elevated to 56.380 U/mL (normal, 0 to about 6.9 kU/L), while serum levels of CA724, CA153 were within the normal range. Liver and

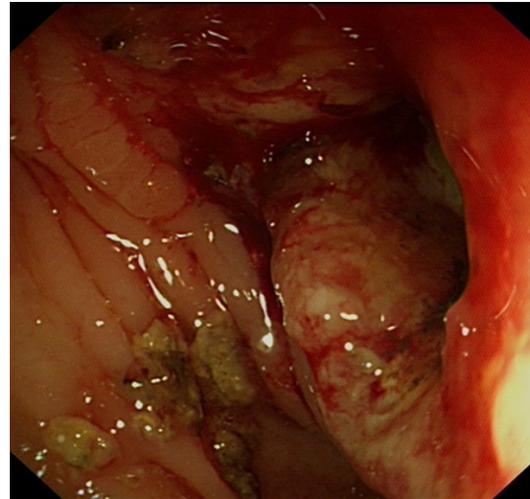


Figure 2. Large intestinal endoscopy showing hard induration and stenosis of the sigmoid.

renal functions were normal. Fecal occult blood test was positive. Large intestinal endoscopy was performed as a further examination in our institute and revealed hard induration and stenosis of the sigmoid, with an extraluminal mass 7 cm proximal to the anal verge (**Figure 2**). The affected mucosal surface was eroded, necrotic, friable and prone to bleeding. Histological findings of the biopsy specimens indicated poorly differentiated adenocarcinoma. Computed tomography (CT) scan of the abdomen revealed eccentric wall thickening of the distal sigmoid colon with a significantly enhanced soft tissue density mass causing an apparent stenosis and nodular low density shadow (**Figure 3**). No sites of distant metastasis were reported on abdominal CT scan.

Finally, it was postulated that the sigmoid tumor was a primary tumor with metastatic adenocarcinoma to the breast which had been removed. After risks, benefits and potential complications were explained, the patient agreed to the procedure. Under thorough observation through laparoscopy, the solitary tumor was found situated in the sigmoid colon and beyond the serosa. Segmental small bowel was fixed at the site of the sigmoid colon cancer. The right ovary was hard and fixation. Thorough macroscopic examination of the liver and rest of the abdomen showed no sign of metastatic disease. Laparoscopy-assisted sigmoidectomy plus segmental small-bowel and ovaries section was successfully performed

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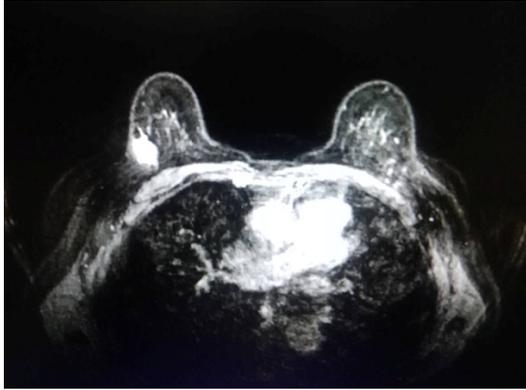


Figure 3. Computed tomography scan of the abdomen.

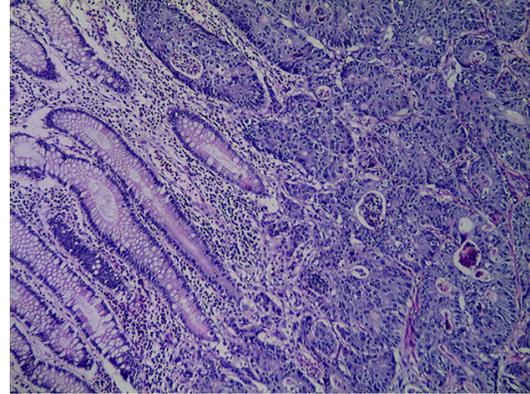


Figure 4. Histopathological examination of the resected specimen (Hematoxylin and Eosin Stain, 100× magnification).

The postoperative course was uneventful, and the patient was discharged from the hospital 9 d after the operation. Histopathological examination of the resected specimen demonstrated that the tumor had invaded to the serosal level and that five regional lymph nodes were metastatic (**Figure 4**). The IHC staining for MLH1, MSH2 and MSH6 were positive. The pathology report showed adenocarcinoma. Therefore, the patient received adjuvant chemotherapy to reduce the risk of cancer recurrence. She received 6 cycles of chemotherapy using S-1. Postoperative abdominal computed tomographic scan and tumor markers (CEA, CA 199) were normal. The patient is still alive 10 months after the second operation.

Literature review

Materials and methods

To identify published and unpublished reports of relevant studies, we searched Pubmed up to April, 2016. In addition, reference lists were checked and related journals and conference proceedings searched manually. Google Scholar was also used to find full texts. Searched terms included the following text: colon cancer, breast, colonic adenocarcinoma, metastasis and so on in several combinations. The search was carried out repetitively until no additional citations could be retrieved. In our study, only English language articles have been reviewed and included.

Results

A total of 32 cases were identified, the earliest being in 1976 (**Table 1**). Most patients were

female (94%), the average age of patients with metastatic breast cancer is 51.1 years (range 28-86 years). On average, breast metastasis is reported to appear 25 months (range 1-10 years) following colorectal cancer diagnosis. Only 3 (10%) cases first presenting as a breast lump or as a breast lump with concurrent colorectal cancer. In our review, we found that most common sites of colon cancer were rectum (6/23). The majority of metastases (48%) were to the left breast (often upper outer quadrant), with 12 (39%) to the right breast, and 4 bilateral (13%). Metastases to the brain, liver, lung, skin, abdominal and axillary lymph nodes, and retroperitoneum were common. Colorectal cancer metastases to the breast averaged 3 cm (range 1-11 cm) in size. In 5 (16%) cases the patients died an average of 14.5 months (range 0.5-48 years) after the diagnosis of breast metastasis, and the remaining 27 were either still alive at the time of the published case report or no survival data was reported.

Discussion

Colorectal carcinoma is the third most common cancer after prostate and lung cancers in men and after breast and lung cancers in women. It is also the third leading cause of cancer-related death after lung and prostate cancers in men and after lung and breast cancers in women [1].

The most common sites of metastases are lymph nodes with 40-70% of cases. Others like liver, lungs, and bone are in descending order. The incidence of concurrent primary colorectal

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Table 1. Colon metastasis to the breast

Author	Age (year)	Gender	Primary colorectal cancer			Metastasis organs	Breast metastasis			Survival
			Time	Stage	Location		Laterality	Size (cm)	Treatment	
Mcintosh 1976 [4]	44	F	1 m	ns	ns	ns	ns	ns	Excision	4 m (Observed)
Lear 1980 [5]	30	F	10 m	Dukes B	ns	ns	Left	3	ns	6 y (Observed)
	67	M	1 y	Dukes B	ns	ns	ns	ns	ns	ns
Nielsen 1981 [6]	59	F	6 m	ns	ns	Liver Peritoneum	Left	2&4	ns	4 m
	68	F	2 y	ns	ns	Peritoneum	Right	3	ns	6 m
Alexander 1989 [7]	28	F	11 m	T4N2	Rectum	-	Right	ns	Excision	4 y (Deceased)
Bhirangi 1997 [8]	86	F	Synchronous	Dukes B	Asecnding	-	Right	2	Wide Local Excision	18 m (Observed)
Muttarak 1998 [9]	36	F	1 y	ns	ns	ns	Bilateral	Multiple	ns	ns
Lal 1999 [10]	69	F	1 y	T3N0	Rectum	-	Left	ns	Wide Local Excision	4 m (Deceased)
Ozakyol 2000 [11]	42	F	6 m	T3	Sigmoid	Retroperitoneal Space Peritoneum	Right	3	Excision	6 m (Observed)
Sironi 2001 [12]	66	F	10 y	T2	ns	Thoracic Skin Lung	Right	ns	Observation	ns
Meloni 2001 [13]	77	F	3 m	T4N2	Cecum	-	Left	2	Excision	6 m (Observed)
Oksuzoglu 2003 [14]	52	F	20 m	T4N2	Sigmoid	-	Left	1.4	biopsy	2 m
Fernandez 2004 [15]	40	F	4	Dukes C	Asecnding	Retroperitoneal Space	Left	4	Mastectomy	6 m (Observed)
Mihai 2004 [16]	53	F	5 y	Dukes B	Rectum	Skin	Left	1	Wide Local Excision	4 m (Observed)
Hisham 2006 [17]	32	F	10 m	T4N2	Rectum	Vertebra Brain	Left	4	Observation	0.5 m (Deceased)
Wakeham 2008 [18]	45	F	2 y	Dukes C	Rectum	Liver Lung	Bilateral	2.2 (Right) 2 (Left)	Observation	ns
	74	F	2 m	Dukes C	Cecum	-	Bilateral	4 (Right) 6 (Left)	Observation	ns
Sanchez 2008 [19]	36	F	4 m	T4	Rectum	-	Left	6	Observation	ns
Ho 2009 [20]	50	M	6 y	T3N1	Asecnding	-	Right	1.5	Observation	1 y (Observed)
Del 2009 [21]	43	F	<1 m	T4N2	Transverse	Liver Bone	Right	4.5	Observation	ns
Barthelmes 2010 [22]	78	F	16 m	T4N0	Transverse	Abdominal Wall	Left	1	Observation	4 m (Deceased)
Noh 2011 [23]	63	F	4 y	T3N1	Sigmoid	Lung	Right	2.8	Wide Local Excision	ns
Perin 2011 [24]	46	F	3 y	T3N1	Sigmoid	Lung	Left	1	Wide Local Excision	16 m (Deceased)
Selcubiricik 2011 [3]	37	F	18 m	T3N0	Sigmoid	-	Left	1	Observation	ns
Shackelford 2011 [25]	44	F	7 y	Dukes A	ns	Brain Lung Mediastinum	Left	11	ns	ns
Santiago 2012 [26]	76	F	8 y	T4N0	Sigmoid	Lung	Left	1.2	Wide local excision	11 y (Observed)
Makhdoomi 2013 [27]	28	F	Synchronous	T4N2	Rectum	-	Bilateral	Multiple	ns	2 m (Observed)
Ahmad 2014 [28]	28	F	Synchronous	T4N2	Rectum	Liver	Right	2	Observation	ns
Vakili 2014 [29]	38	F	15 m	T3N1	Asecnding	Ovarian	Left	9	Mastectomy	8 m (Observed)
Kothaida 2015 [30]	45	F	ns	Stage 4	Asecnding	-	Right	0.68 & 0.9	Observation	ns
	56	F	ns	Stage 4	ns	Liver	Right	1.46	Observation	ns

ns, not stated.

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cancer with secondary breast metastasis is very low.

Primary breast cancer is the most common cancer afflicting women. Metastases to the regional lymph nodes are found at the time of resection, with metastases to more distant sites occurring most frequently in bone, lungs, and the liver [31]. Metastatic cancer to the breast is very rare. Metastatic breast tumors are even rarer from colonic adenocarcinomas. Here we report a new case. Because of the rare incidence, physicians lack the knowledge of and vigilance towards colorectal breast metastases. This situation may lead to misdiagnosis and delay in treatment. In the present patient, the symptoms of secondary breast cancer found by conventional preoperative examination. When the histopathologic examination of the core biopsy samples revealed invasive adenocarcinoma, further systemic examinations should be conducted. The surgeon cannot simply be satisfied with a single diagnosis and the examination like abdominal CT scan, gastrointestinal endoscopy and the serum tumor markers test are necessary to avoid misdiagnosis.

When breast nodules are found in a patient, how to distinguish between the primary cancer and the metastasis of colorectal cancer warrants attention. Imaging evaluation which includes sonography and mammography can be useful in the differential diagnosis of primary versus secondary breast cancer [3]. On sonography, metastatic breast lesions usually appear hypoechoic nodules with indistinct and irregular margins. Penetrating vascularity is variable, but the presence of this finding is very suggestive for malignancy [20]. According to the literature, the Mammographic for a secondary breast cancer is usually a rounded and well-circumscribed mass which do not cause an overlying skin or nipple retraction [22, 32]. They often have specific features and can mimic benign lesions. It was reported that micro calcifications are found rarely in metastasis from the colon other than breast origin [16]. But generally, micro calcifications do not exclude the possibility of metastasis.

The standard of care is to evaluate the tissue sample through ultrasound guided core needle biopsy of the lesion. It is recommended that

the core biopsy is comparatively better than fine needle aspiration biopsy with the reason that the core biopsy is more diagnostic sensitivity and specificity and present more tissue architecture. Core biopsy allows histological assessment of the tissue, helping in identifying the origin of the carcinoma [20]. On the histologic finding, a lack of elastosis due to their fast growth, a sharp transition at the border of the tumor and the periodical and peribulbar location of the tumor with the absence of in situ ductal carcinoma favor a metastasis [2].

Immunohistochemical (IHC) studies are always recommended to establish the histological type as well as the tumor origin. Cytokeratin 7 (CK7) and cytokeratin 20 (CK20) are the most widely used to establish an accurate final diagnosis [33]. The majority of the primary ductal adenocarcinomas of breast are CK7 (+) and CK20 (-), while most colorectal carcinomas are usually CK7 (-) and CK20 (+). Additionally, positive immunostaining for CDX2 and CK20 and negative for ER, PR, Her2, GCDP15, BCA, and CK7 are highly sensitive and specific for colonic cancers metastatic to the breast [34].

It is important to distinguish metastatic colorectal carcinoma to the breast from a primary mammary carcinoma. Because the management of patients with colorectal carcinoma to the breast is extremely complex and depends upon multiple factors such as general condition of the patients, primary colorectal tumor, lymph node status and so on. Since metastatic breast cancer indicated that the colorectal carcinoma is in highly aggressive disseminated status and associated with a poor prognosis, some doctor advocated that surgical excision should be avoided in the view of short life expectancy and risk of seeding to the skin [22]. Other doctor suggested that excisional biopsy was usually appropriate and provided adequate local control [35]. Most literature reported that patients were firstly diagnosed the colon cancer and at the same time or after the metastatic breast tumors were found. After risks, benefits and potential complications were considered, some tumors in breast were removed and the others were not. Since our 80-year-old male patient whose endoscopy indicated stenosis of the sigmoid that would lead to obstruction of colon, the operation was necessary.

Conclusion

In conclusion, the incidence of metastatic colorectal carcinoma to the breast is relatively low. When the breast tumor which is suspicious metastasis is found, a meticulous examination of every organ should be conducted until no other malignant tumor is found. Besides exploring the detailed clinical background, an appropriate radiologic evaluation is extremely important in the initial triage of any breast lesion and also helps identify any occult malignancy. The management of patients with colorectal carcinoma to the breast depends upon multiple factors. Whether operated or not, according to the pathological type and stage of the tumors, appropriate adjuvant chemotherapy should be given. Metastatic colorectal carcinoma to the breast often occur in the setting of disseminated disease and the prognosis is poor.

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Disclosure of conflict of interest

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Address correspondence to: Dr. Chun Song, Gastrointestinal Surgery, Shanghai East Hospital, Tongji University School of Medicine, 150 Jimo Road, Shanghai 200120, P. R. China. Tel: (8621)38804518; E-mail: chunsong163@163.com

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