CASE REPORT

Gastric signet-ring adenocarcinoma presenting with breast metastasis

Anastasios L Boutis, Charalambos Andreadis, Frideriki Patakiouta, Despina Mouratidou

Abstract
Breast metastases from gastric cancer are extremely rare. A case report of a 37-year-old female with breast inflammatory invasion and ascites is described. Breast biopsy revealed carcinomatous invasion of the lymphatics from adenocarcinoma cells with signet-ring features. Estrogen (ER) and progesterone receptors (PR) and c-erb-B2 were negative. Upper gastrointestinal endoscopy revealed a prepyloric ulcerative mass. Histopathologic examination of the lesion showed infiltration from a high-grade adenocarcinoma, identical with that of the breast. Immunostaining was positive for cytokeratins CK-7 and CK-20 and CEA and negative for ER and PR. Ascitic fluid cytology was positive for adenocarcinoma cells. Mammography was not diagnostic. Abdominal CT scanning revealed large ovarian masses suggestive of metastases (Krukenberg’s tumor). A cisplatin-based regimen was given but no objective response was observed. The patient died six months after initial diagnosis. A review of the literature is performed.

© 2006 The WJG Press. All rights reserved.

Key words: Gastric adenocarcinoma; Signet-ring; Breast metastasis; Ovarian metastasis

Boutis AL, Andreadis C, Patakiouta F, Mouratidou D. Gastric signet-ring adenocarcinoma presenting with breast metastasis. World J Gastroenterol 2006; 12(18): 2958-2961

http://www.wjgnet.com/1007-9327/12/2958.asp

INTRODUCTION
Breast metastases from extra-mammary neoplasms are extremely rare. The incidence ranges between 1%-2% in clinical and 1.7%-6.6% in autopsy series[1-2]. Less than 500 cases of secondary breast tumors have been reported so far in the English speaking literature[3]. The most common primary malignancies metastasizing to the breast are malignant melanoma, lung cancer, carcinoid tumors, ovarian cancer, renal cancer, gastrointestinal carcinomas and a variety of other primaries[3-5]. Herein, a case of a woman with gastric signet-ring adenocarcinoma presenting with breast metastasis is described.

DISCUSSION
Metastatic breast involvement from extra-mammary
Breast invasion is the initial manifestation of the disease in 25%-40% of the cases. Mammographically, metastatic tumors in the breast present as well-circumscribed nodules without microcalcifications, mimicking benign breast lesions. Calcifications may be seen in metastatic deposits from ovarian carcinoma with psammoma bodies. The most common localization of metastatic lesions is the upper-outer quadrant of the left breast. Breast involvement is bilateral in 25% of the cases, and there is concomitant axillary lymph node enlargement in up to 15%. The occurrence of multiple tumor nodules is unusual and diffuse involvement mimicking inflammatory breast carcinoma is rare. The latter clinical manifestation, due to lymphatic invasion, is rapidly progressive, and may produce clinical signs of breast involvement before a firm metastatic nodule is formed, which is even more common in hematological malignancies (leukemias, lymphomas).

Breast metastases from gastric cancer are extremely rare. To date, only 25 cases have been reported in the English speaking literature and are mentioned in Table 1. Signet-ring features have been reported in 13 cases. From reports with available data, it seems that breast involvement usually follows the detection of gastric carcinoma. Breast metastasis as initial manifestation of a primary gastric tumor, as in our case, has been reported in 10 cases. In half of these cases breast involvement had the clinical appearance of inflammatory breast cancer.

Breast metastases from gastric carcinoma differ from primary breast cancer in their histopathologic characteristics. Immunostaining is usually negative for estrogen and progesterone receptors, as well as for c-erbB-2. GCDFP-15 (gross cystic disease fluid protein-15) is also absent. There is no evidence of an in situ component and a lack of desmoplastic response. On the contrary, lymphatic tumor emboli and epithelial markers like CK7, CK20 and CEA are usually present.

In our case, the presence of signet-ring cells within breast lymphatics, the absence of mass or microcalcifications in the mammography, the lack of an in situ component and hormone receptor negativity strongly suggested an extra-mammary primary. It is of noted interest that Steinbrecher and Silverberg in 1976 first described primary signet-ring carcinoma of the breast, as a subtype of lobular carcinoma, with aggressive biological behavior and an increased tendency to metastasize in the abdomen and in the gastrointestinal tract compared to other histological subtypes. Signet-ring carcinoma of the breast metastatic to the stomach has also been reported.

The presence of cystic ovarian masses suggested metastatic ovarian involvement (Krukenberg's tumor). Unfortunately, the patient's unfavorable clinical condition did not allow histological confirmation. Metastatic involvement of the breast and the ovaries is extremely rare and has been reported in only 5 cases so far. Selective invasion of hormone-dependent organs seems quite intriguing, especially in pre-menopausal women. Increased blood supply of the breast has been proposed as the
mechanism for the increased incidence of breast metastasis in pre-menopausal women. On the other hand, gastric cancer seems to have a more aggressive biologic behavior in younger age groups, where hormonal factors are implicated. The appearance of breast metastases in men with gynecomastia supports the latter hypothesis. In our patient, hormonal therapy for the induction of ovulation may have influenced the natural history of the disease. However, no conclusions about the pathogenesis of the phenomenon can be drawn.

Metastatic disease of the breast is rare, and usually has atypical clinical and mammographic presentation. In cases of breast inflammation or lumps, biopsy should be performed, even in the presence of an extra-mammary neoplasm. Likewise, peculiar histological features from malignant breast lesions should be co-estimated with other clinical parameters toward the diagnosis of metastatic disease. Thus, avoidance of unnecessary radical surgical procedures and an adequate treatment is more probable to be given in these patients.

REFERENCES

1 Di Cosimo S, Ferretti G, Fazio N, Mandala M, Curigliano G, Bosari S, Intra M, Latronico A, Goldhirsch A. Breast and ovarian metastatic localization of signet-ring cell gastric carcinoma. Ann Oncol 2003; 14: 803-804
2 Hamby LS, McGrath PC, Cibull ML, Schwartz RW. Gastric carcinoma metastatic to the breast. J Surg Oncol 1991; 48: 117-121
3 Madan AK, Ternovits C, Huber SA, Pei LA, Jaffe BM. Gastrointestinal metastasis to the breast. Surgery 2002; 132: 889-893
4 Vizcaíno I, Torregrosa A, Higueras V, Morote V, Cremades A, Torres V, Olmos S, Molins C. Metastasis to the breast from extramammary malignancies: a report of four cases and a review of the literature. Eur Radiol 2001; 11: 1659-1665
5 Alexander HR, Turnbull AD, Rosen PP. Isolated breast metastases from gastrointestinal carcinomas: report of two cases. J Surg Oncol 1989; 42: 264-266
6 Barai S, Kumar R, Haloi AK, Dhanpati, Banopadhya G, Malhotra A. Bone scan demonstrating metastasis to the breast from an ovarian carcinoma and a review of the literature. Clin Nucl Med 2004; 29: 167-170
7 Domanski HA. Metastases to the breast from extramammary neoplasms. A report of six cases with diagnosis by fine needle aspiration cytology. Acta Cytol 1996; 40: 1293-1300
8 Kwak JY, Kim EK, Oh KK. Radiologic findings of metastatic signet ring cell carcinoma to the breast from stomach. Yonsei Med J 2000; 41: 669-672
9 Raju U, Ma CK, Shih A. Signet ring variant of lobular carcinoma of the breast: a clinicopathologic and immunohistochemical study. Mod Pathol 1993; 6: 516-520
10 Merino MJ, Livolsi VA. Signet ring carcinoma of the female breast: a clinicopathologic analysis of 24 cases. Cancer 1981; 48: 1830-1837
11 Steinbrecher JS, Silverberg SG. Signet-ring cell carcinoma of the breast. The mucinous variant of infiltrating lobular carcinoma? Cancer 1976; 37: 828-840
12 Yim H, Jin YM, Shim C, Park HB. Gastric metastasis of mammary signet ring cell carcinoma--a differential diagnosis with primary gastric signet ring cell carcinoma. J Korean Med Sci 1997; 12: 256-261
13 Park CH, Whang HS, Park HB. Bilateral signet-ring cell carcinoma of the breast: scintigraphic findings. Clin Nucl Med 1996; 21: 115-117

14 Howarth CB, Caces JN, Pratt CB. Breast metastases in children with rhabdomyosarcoma. Cancer 1980; 46: 2520-2524

15 Kwan WH, Choi PH, Li CK, Shing MK, Chik KW, Yuen P, Chow LT. Breast metastasis in adolescents with alveolar rhabdomyosarcoma of the extremities: report of two cases. Pediatr Hematol Oncol 1996; 13: 277-285

16 Maeta M, Yamashiro H, Oka A, Tsujitani S, Ikeyuchi M, Kajbara N. Gastric cancer in the young, with special reference to 14 pregnancy-associated cases: analysis based on 2,325 consecutive cases of gastric cancer. J Surg Oncol 1995; 58: 191-195

17 Cappabianca S, Grassi R, D’Alessandro P, Del Vecchio A, Maioli A, Donofrio V. Metastasis to the male breast from carcinoma of the urinary bladder. Br J Radiol 2000; 73: 1326-1328