Widespread Microscopic Gastrointestinal Metastases: An Unusual Manifestation of Breast Cancer

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INTRODUCTION

Melanoma and breast cancer, respectively, are the malignancies which most often metastasizes to the gastrointestinal (GI) tract in females. Lobular breast cancer has been linked with upper gastrointestinal tract metastases while ductal breast carcinoma metastases are more frequently associated with the liver, lung and brain.

Past case reports have presented metastatic disease involving the lumen of the GI tract. Those patients, however, had previously known breast cancer or direct visualization of metastatic disease either with endoscopy or radiography. We describe a case of diffuse microscopic gastrointestinal metastases as the initial manifestation of breast cancer.

CASE REPORT

A 55 year old white female presented with several months of nausea, vomiting and diarrhea. The nausea was worse during the morning and was associated with bilious emesis. Her past medical history included hypertension, gastroesophageal reflux disease, atypical migraines, osteoarthritis, pulmonary embolism at the age of 25 years and aortic stenosis due to a bicuspid valve, leading to aortic valve replacement in 2009. She had a known family history of breast cancer (two maternal aunts and maternal grandmother). She had been taking metformin for years, without GI

Figure 1. Colonic mucosa is notable for diffuse cellular infiltrate in the lamina propria; individual cells demonstrate avacuolated cytoplasm, enlarged nuclei and prominent nucleoli. (Hematoxylin and eosin; overall magnification x 25).

Figure 2. Clusters of epithelial cells staining positive for Estrogen Receptors. (Immunohistochemical staining for ER; overall magnification x 25).
symptoms, and estrogen replacement since age 37 years following a total abdominal hysterectomy with bilateral oophorectomy for non-malignant disease. At the time of her presentation, her abdominal examination was normal. Routine blood chemistry and urine analysis were unremarkable.

Due to the severity and persistence of her GI symptoms, she underwent endoscopic evaluation. Colonoscopy demonstrated a diminutive hyperplastic polyp. Otherwise, the gastric, duodenal and colonic mucosa appeared normal. Random biopsies taken from all three locations contained malignant cells (Figure 1) that stained positive for Estrogen Receptors (Figure 2), Progesterone Receptors (Figure 3), GCDFP-15 (Figure 4) and Mammoglobin (Figure 5). CD138, CD45, CD20, CD3, S-100 and HER2/neu stains were negative. These stains were indicative of adenocarcinoma of breast origin. Of note, screening mammography performed 6 months prior to presentation only demonstrated multiple calcifications that were unchanged from years prior and was interpreted as consistent with fibrocystic breast disease.

Breast examination and repeat mammography were again consistent with fibrocystic breast disease without evidence of any discrete mass. Neither positron emission tomography (PET) nor whole body bone scintigraphy revealed metastases. Serum CA 27-29 level was elevated at 448 units/ml (normal < 38 units/ml).

The patient has received four cycles of Docetaxel (Taxotere) and Cyclophosphamide (Cytoxan) followed by maintenance therapy with Letrozole (Femara). Her gastrointestinal symptoms have resolved with chemotherapy.

DISCUSSION

Fourteen to 35% of patients who die from breast cancer are found to have luminal gastrointestinal involvement at the time of autopsy. 2-5 Gastric involvement has been found in 2 to 18% of such autopsies. 2-6 However, only 0.3% of living patients have gastric metastases. 3-5 The reasons for much lower identification of GI metastases may include vagueness or absence of GI symptoms, attribution of these symptoms to chemotherapy or the decision to avoid invasive testing in patients with advanced disease.

Whereas lobular carcinoma of the breast accounts for only 10% of all breast cancer cases, it accounts for 64% of luminal metastatic disease, and specifically 70

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to 86% of gastric involvement.2,3,7 Such metastases are almost always found years after the primary cancer was discovered.

Luminal metastatic disease usually appears grossly as discrete nodules or linitis plastica, thus mimicking gastric carcinoma.3 Moreover, microscopic examination of these lesions often shows a signet-ring pattern that can also be mistaken for gastric carcinoma. It is therefore imperative that immunohistochemical analysis be performed on these tissues in order to distinguish breast from gastric origin as this affects prognosis and treatment.3,5,6,8,9,10

Patients who are diagnosed with luminal metastases of the GI tract from breast cancer respond well initially to chemotherapy but have a life expectancy of only 10 to 28 months.4,11 Surgery is not indicated in these patients.

To our knowledge, this is only the second case report of breast cancer presenting de novo as luminal metastases.8 In all other reports, patients presenting with luminal metastases had previously discovered primary breast cancer. However, in the other de novo case, the primary site was identified.8 In our case, the primary site of cancer could not be found. The finding in our patient of extensive metastases throughout the luminal tract with no gross abnormality is also a rare finding. Her disease was discovered only because multiple random biopsies were obtained.

Our case highlights several pertinent clinical points. First, clinicians must be aware that lobular breast cancer has a high incidence of metastases to the GI tract. Any patient with a history of breast cancer, even if remote, who presents with GI symptoms should therefore receive consideration for endoscopy in order to evaluate for metastatic disease. Moreover, if such patients have a normal gross examination of the upper and lower GI tracts, random biopsies are recommended to rule out occult metastatic disease. Lastly, if malignant cells are identified, immunohistochemical analysis should then be performed in order to differentiate between metastatic versus primary disease.

References