Peer-Reviewed

Breast Cancer Metastasis to the Colon Presenting After Fifteen Years

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Second year student members (non-Delegate) were given the opportunity to apply for a travel grant to attend an upcoming Fall Conference or Spring Meeting of their choice. Students were required to write a manuscript, and the winning entry received a grant valued at up to $1600 (full week registration + $1000 to help cover travel expenses). Congratulations, Samantha, on your winning submission!

New CE Article

Abstract

The case presented is that of a female in her late 70s with a history of invasive ductal carcinoma, diagnosed in 2002. Fifteen years later, she was found to have metastases to the stomach and to the colon, both rare sites of spread from breast cancer. The metastasis to the colon is of particular note here as it was received as a surgical specimen and evaluated by a pathologists' assistant. Histologically, the cell morphology was compared between the primary breast cancer and colon metastasis and found to be strikingly similar. Further discussed are related case reports and analyses in the literature of such breast cancer metastases to the gastrointestinal tract and their characteristics. Although rare, the possibility of gastrointestinal metastasis in a patient with a history of breast cancer should always be considered when diagnosing or grossing a gastrointestinal lesion.

Keywords: ductal carcinoma of breast, breast cancer metastasis, gastrointestinal metastasis, metastasis to colon

Introduction

Reports of breast cancer metastasizing to the gastrointestinal tract are quite rare, and even rarer to have occurred in the colon. Most often, breast cancer metastasizes to the lymph nodes, bone, lungs, liver, and brain. The case presented here is that of a patient with a history of invasive ductal breast cancer metastasizing fifteen years later to the colon, and is significant for several unusual findings in its presentation and pattern of metastasis when compared to the literature.

Case Presentation

A Caucasian woman now in her late 70s had a diagnosis of breast cancer in 2002 and underwent a left modified radical mastectomy and axillary node dissection, 6/14 of which were positive, but no other metastases were identified at the time. The tumor was 3.5 cm in greatest dimension. The cancer was diagnosed as moderately differentiated invasive ductal carcinoma, estrogen receptor (ER) positive, progesterone receptor (PR) weakly positive, and HER2/neu negative. Following treatment with chemotherapy and antihormonal therapy, she had been periodically monitored and had no evidence of recurrence.

In late 2017, fifteen years after the original breast cancer diagnosis, the patient presented to the emergency department with nausea, vomiting, and inability to keep down food or liquid. Endoscopy revealed a gastric outlet obstruction. A biopsy of the antrum was positive for cancer, determined to be metastases of her previous ductal breast cancer by use of immunohistochemistry comparison. Computed tomography (CT) scans revealed marked abnormal thickening of the pylorus and dilation of the stomach, but no other indications of metastasis. A palliative bypass with gastrojejunostomy was performed followed by a chemotherapy regimen.

Three months later, the patient returned to the emergency department complaining of abdominal pain, nausea, and vomiting that had been worsening over the past few days. She also had worsening abdominal distension and reported no bowel movements for the past four days. A CT scan revealed the cecum was dilated to greater than 12 cm, a large left lower quadrant abdominal wall hernia, and a right inguinal hernia containing multiple loops of small bowel. The patient was admitted and exploratory surgery was recommended by the surgeon, as a colonoscopy was unable to be performed. It was theorized by physicians that a loop of colon may be trapped within the hernia, causing the cecal distension.

The surgery revealed several remarkable findings. The cecum was very distended and believed to be perforated within the hernia. The hernia sac contained a large amount of purulent fluid and thickened loops of small bowel, as well as a large portion of omentum and stool. The ascending colon and hepatic flexure were constricted, completely blocking the area extending to the transverse colon. A right hemicolectomy and repair of the left side Spigelian hernia was performed.

Pathological Findings

Upon gross examination of the surgical specimens, the pathologists' assistant noted 15 cm of the ascending colon wall was narrowed and thickened with congested mucosa imparting a cobblestone appearance, giving the gross impression of Crohn's disease or another inflammatory colitis (**Fig. 1, 2**). The cecum was dilated and the mucosa flattened. The hernia sac was remarkable for a nodule containing exudate upon sectioning. Appropriate sections including the cobblestoned areas,

Fig. 1: Wall of colon specimen showing cobblestone arrangement of metastatic tumor (previously sectioned).

Fig. 2: Cobblestoned portion of colon wall cut to reveal infiltration of the lesion into the mucosal layers.

dilated cecum, unremarkable mucosa, and attached appendix were submitted for histological examination.

Microscopically, the cobblestoned portion coincided with diffusely infiltrating and poorly differentiated carcinoma resembling linitis plastica. Neoplastic cells with signet-ring forms involved the mucosa and bowel wall and invaded into the pericolic tissue and serosal surface. There was also evidence of neoplastic cells in grossly uninvolved portions, including the dilated cecum. Two pericolic lymph nodes found around the cobblestoned portion and the nodule in the hernia sac were positive for metastatic carcinoma.

Immunohistochemistry staining determined the tumor to be ER positive and PR negative. HER2/neu testing was not performed. Slides from the patient's previously diagnosed breast cancer were obtained from the original treating hospital and compared with the metastatic tumor, which showed the two to have similar histological features, though the colon metastasis was diffuse and poorly differentiated in comparison (**Fig. 3, 4**). The final diagnosis was metastatic breast carcinoma, diffusely involving the right colon.

The patient tolerated the procedure well and after recovery was discharged and continued to be treated in outpatient care. Two months later, she was admitted to the emergency department with worsening renal function and elected to undergo supportive care. As of the submission of this manuscript, the patient had been transferred to a hospice facility.

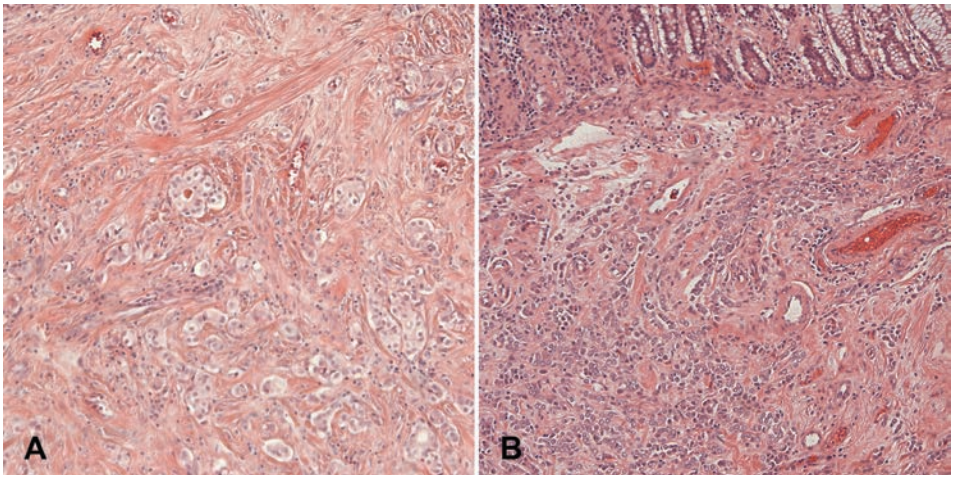

Fig. 3: Comparison of primary invasive ductal breast cancer (A) and colon metastasis taken from cobblestoned area (B), low magnification (H&E).

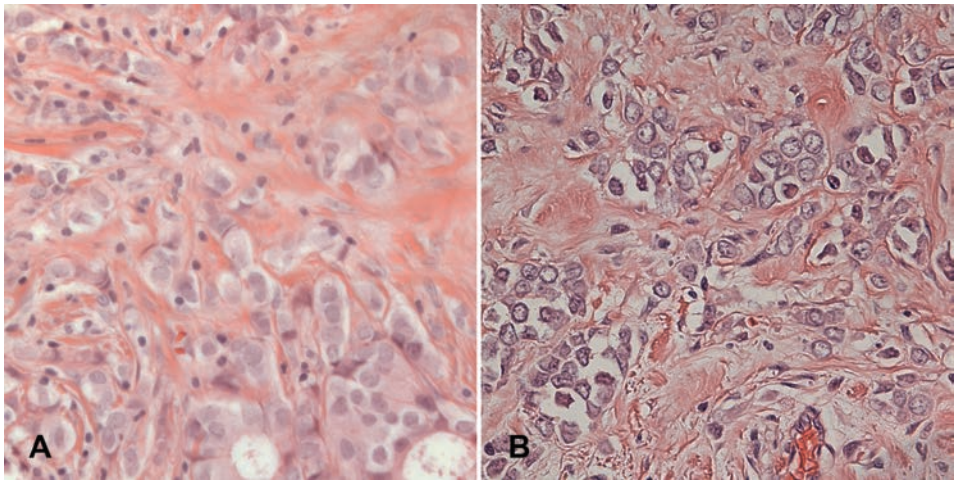

Fig. 4: Comparison of primary invasive ductal breast cancer (A) and colon metastasis taken from cobblestoned area (B), high magnification (H&E).

Discussion

This case is noteworthy for demonstrating several rarities in regard to breast cancer metastases, all of which raise important diagnostic challenges for health care providers to consider. First, reports of breast cancer metastasizing to the gastrointestinal tract are rare, and even more rare to have occurred in the colon. Most often, breast cancer metastasizes to the lymph nodes, bone, lungs, liver, and brain. In a five-year retrospective study at one institution, of 980 patients diagnosed with breast cancer only five (0.5%) had metastatic disease to the gastrointestinal tract.[1] The same study found in their case analysis and in a review of literature that the stomach was the most common site of gastrointestinal metastasis from breast cancer (60% of cases), while the colon was indicated in 11% of cases. It is likely that the incidence of gastrointestinal metastasis from breast cancer may be higher due to clinically undetected cases, as evidenced by a study comparing surgical cases with autopsy results that found over twice as many incidences of gastrointestinal metastases at autopsy than were clinically detected in surgical cases.[2]

Despite being the most common type of invasive breast carcinoma, ductal carcinoma is less likely to metastasize to the gastrointestinal tract than lobular carcinoma. In published reports, lobular breast carcinoma is the most often reported type implicated in gastrointestinal metastasis from the breast, though reasons for this have not yet been explored.[1] A study comparing metastatic patterns of lobular and ductal breast carcinoma found gastrointestinal metastases in 4.5% of patients with lobular diagnoses and only in 0.2% of ductal.[3]

The gross and microscopic characteristics of the presented case do coincide with published reports. The appearance of breast cancer metastases to the gastrointestinal tract have been found to be variable; one study revealed a range of presentations, from diffuse thickening of the walls mimicking linitis plastica to large obstructive ulcerated masses.[2] Any of these presentations may cause diagnostic difficulty, as the metastasis may be mistaken for either a gastrointestinal primary cancer or other inflammatory disease. There have been two published reports of metastasis to the colon specifically mistaken for Crohn's disease based on clinical, surgical, and/or radiographic findings.[4,5] Complicating a proper diagnosis is the variety and non-specificity of gastrointestinal symptoms, typically including nausea, vomiting, diarrhea, and intestinal pain.[1] Many of these symptoms also coincide with side effects of treatment, further obscuring the diagnosis.

Microscopically, most reports note a signet-ring cell pattern of morphology in gastrointestinal metastases, regardless of whether the original breast cancer was ductal or lobular.[2] In one of the reported cases of metastasis simulating Crohn's disease, the morphology also showed signet-ring cell configuration.[5] In the presented case, the receptor status changed from ER/PR positive in the primary tumor to ER positive, PR negative in the metastatic tumor. While in most cases immunohistochemistry results match between the original breast cancer and metastasis, there have been

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reported cases with a change in receptor status, especially in poorly differentiated cancers that tend to lose the tissue-specific gene expression apparent in the primary tumor.[6]

The time elapsed between the original breast cancer diagnoses and discovery of gastrointestinal metastasis is also long in this case at 15 years; however, lengthier time spans have been recorded. Metastases from breast cancer occur within the first five years following the diagnosis of early stage disease about 75% of the time.[7] In the case of gastrointestinal metastasis, analyses of published reports have discovered median time intervals between 4-7 years, but there have been cases of gastrointestinal metastasis reported up to 30 years later.[7] In the aforementioned five-year retrospective study, the range of time between breast cancer diagnosis and discovery of metastasis to the gastrointestinal tract was between 0 (found at initial diagnosis) and 22 years.[1] Unfortunately, the diagnosis of gastrointestinal metastasis from cancer of any kind is followed by a poor prognosis, with most patients surviving no more than a year.[2]

The patient's previous history of breast cancer was not provided to the pathologists' assistant before grossing the specimen, as it was diagnosed at a different hospital 15 years prior. Had the history been available, the colon specimen may have been grossed differently. First, guidelines for breast cancer grossing would have been followed, including ensuring proper fixation time of the specimen. Believing the specimen to be affected by an inflammatory process rather than a tumor, a thorough search for lymph nodes was not performed, another change that would have been made if the history or possibility of cancer was known. The specimen may also have been sampled differently, perhaps by sampling more of the grossly unaffected areas, rather than taking the majority of samples from the cobblestoned portion. Overall, the grossing procedure did not affect the outcome of this case, as it was still able to be diagnosed properly with no additional sampling required.

In conclusion, this case brings up two important points for providers. First is the potential for breast cancer to metastasize to the gastrointestinal tract, no matter how rare it is believed to be, nor the span of time since the original diagnosis. In any patient with a history of breast cancer presenting with gastrointestinal lesions discovered surgically or radiographically, the possibility of metastasis should be considered. Second, this case stresses the importance of the pathologists' assistant to be provided with patient history so appropriate sections are taken. In the presented case, immunohistochemistry was ordered so the origin of the colon tumor was discerned, and when combined with histological comparison of the primary breast tumor, accurate diagnosis was made. Despite the rarity of this event, this case as well as the handful of published literature have in common the goal to bring the possibility of colon and other gastrointestinal metastases from breast cancer closer to the forefront of providers' minds. ■

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