

METASTATIC INVASIVE DUCTAL BREAST ADENOCARCINOMA TO THE GALLBLADDER AND COLON IN AN 80 YEAR OLD OBESE FEMALE: A CASE REPORT

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SIGNIFICANCE:

Breast cancer is one of the most devastating cancers afflicting women, being a main cause of cancer related death. Approximately 50% of these patients have developed regional or distant metastases at the time of diagnosis; hence, an early diagnosis and surgery with indicated neoadjuvant therapy are crucial in eradicating this disease and improving patient survival.

CLINICAL PRESENTATION:

We report a case of an 80 yo morbidly obese female who was diagnosed with metastatic Invasive ductal Ca (ER, PR positive, Her-2/neu negative and Ki67 positive) of the breast who developed metastasis to the colon and gallbladder 11 months after diagnosis.

MANAGEMENT:

The patient did not consent for mastectomy and chemotherapy initially. 5 months after, she had an elective cholecystectomy revealing a metastatic breast carcinoma to the gallbladder (ER positive, PR negative, Her-2/neu positive and Ki-67 positive. For 8 months she was only receiving Denosumab for the bone metastasis until 2 months later when she started to complain of changes in her bowel movement hence a colonoscopy was done revealing a biopsy consistent with a poorly differentiated metastatic breast carcinoma to the colon (ER positive, PR negative, Her-2/neu positive and Ki-67 positive. Currently patient is receiving Herceptin.

RECOMMENDATION:

Metastatic disease should be considered when a patient experiences GI symptoms with a history of breast cancer or conversely primary breast cancer should be thoroughly searched in case of metastasis to GI or biliary tract.

Keywords:

Invasive ductal breast carcinoma, estrogen and progesterone receptor positive, Ki-67, Her-2/neu

SUMMARY:

Breast carcinoma is the most common malignancy of women worldwide. It is most commonly associated with metastases to the liver, lung, bone, and the brain. Invasive ductal carcinoma is the most common histologic type and constitutes 65 to 85% of all breast cancers. Metastatic involvement of the gastrointestinal

tract secondary to breast cancer is rare. Gallbladder and colonic metastasis involving almost the entire colon from breast cancer is even rarer. Metastatic breast carcinoma involvement of the gastrointestinal tract is usually of the lobular histologic subtype. To the best of our knowledge, the case presented here is one very rarely reported in literature, showing

gallbladder and colonic metastasis from invasive ductal breast cancer.

INTRODUCTION:

Breast cancer is one of the most devastating cancers afflicting women, being a main cause of cancer related death. Approximately 50% of these patients have developed regional or distant metastases at the time of diagnosis; hence, an early diagnosis and surgery with indicated neoadjuvant therapy are crucial in eradicating this disease and improving patient survival. Likewise gastrointestinal metastases from primary breast carcinoma are rare but more common in invasive lobular carcinoma than invasive ductal carcinoma. The symptoms may be non-specific and the presentation can occur many years after the initial primary breast carcinoma. Radiological and endoscopic findings can be difficult to distinguish from inflammatory bowel disease and primary carcinoma of the GI tract. Histological and immunohistopathology assessment will definitely confirm the diagnosis of metastatic breast carcinoma.

CLINICAL PRESENTATION:

The patient was an 80-year-old female with a history of right breast mass, chronic low back pain and asymptomatic cholelithiasis who underwent ultrasound-guided core needle biopsy revealing an invasive ductal adenocarcinoma and bone scintigraphy scan showing osseous metastasis in the skull and ribs. This patient also has history of recurrent pleural effusion with unremarkable cytology of the pleural fluid. Elective cholecystectomy was done revealing a gallbladder with histomorphologic and immunohistochemistry (Mamaglobin positive, GATA3 positive, Ki67 positive and ER positive, PR negative, Her2/Neu positive) consistent with

metastatic breast carcinoma. The primary tumor was identified as an invasive ductal carcinoma of the breast that was estrogen receptor (ER) positive (+++), and progesterone receptor positive (+++). Immunohistochemical markers indicated that the carcinoma was c-erbB-2 (HER2/neu) negative, and Ki67 positive (20%). The patient was advised to undergo chemotherapy and surgery but did not consent initially. She was only receiving Denosumab for the bone metastasis. During the interim, patient had recurrent episodes of right sided pleural effusion and repeated thoracentesis with negative cell cytology. Until 11 months after; she started to have alterations in her bowel movement described as frequent watery stools. PET scan revealed hypermetabolic enlarged right paratracheal lymph node, hypermetabolic lytic focus on the manubrium sterni and diffuse FDG bone marrow activity in the axial and appendicular skeleton all worrisome for metastasis. The colon and rectum was not evaluated due to absence of rectal contrast material precluding adequate evaluation. Colonoscopic findings revealed a congested mucosa with poor vascularity and multiple sessile and subpedunculated polyps located adjacent to each other from the rectum up to the ascending colon. (see figure 1 & 2)

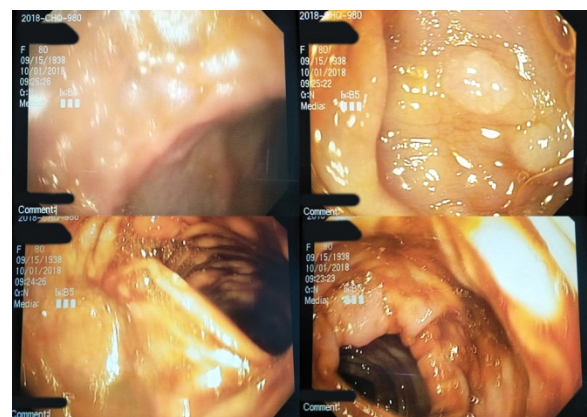


Figure 1. random photos of the colon showing congested mucosa

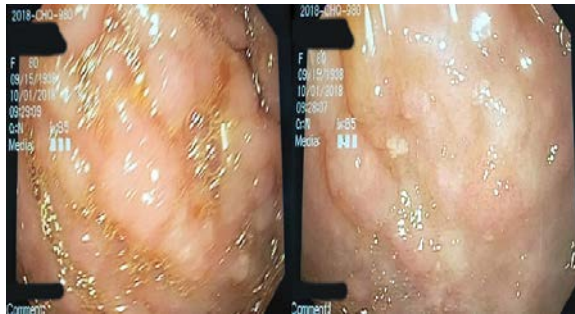
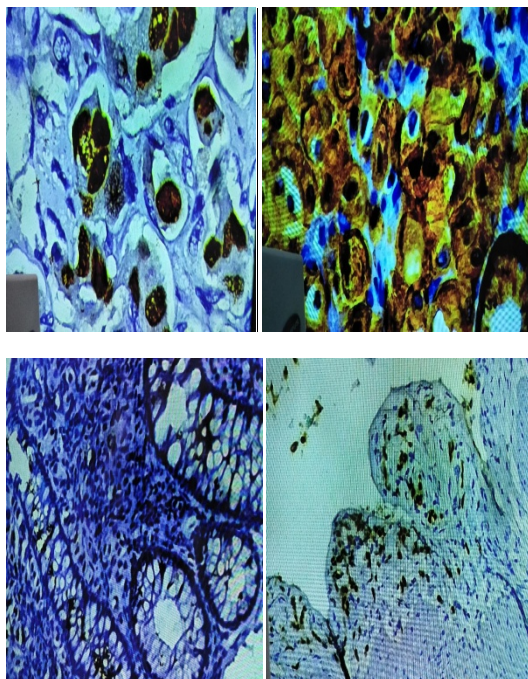


Figure 2. polypoid sessile polyps noted from the ascending, descending and sigmoid colon.

Histopathology revealed a poorly differentiated metastatic carcinoma with the following immunohistochemistry findings consistent with metastatic breast adenocarcinoma: ER positive, PR negative, Her2/neu receptor positive, Ki67 index 17.95%, GATA3 positive and mammoglobin positive. (see figure 3)



DISCUSSION:

Invasive ductal adenocarcinoma of the breast is frequently associated with loco-regional and distant metastases. Generally, breast cancer metastasis to the colon is hematogenous, although it may also result from dissemination of tumor cells by peritoneal and regional lymphatic routes. In one well aligned study, colon metastases were found in only 3% of patients (20 of 720 cases)¹ which is less frequently uncovered than upper gastrointestinal tract². Fewer reports described rectal metastases from breast cancer^{3,4,5} although synchronous rectal metastases in addition to other sites have also been recognized.⁶ Rarely, hepatobiliary tract involvement exists^{3,7}. One particular feature of gastrointestinal manifestations of metastatic breast cancer is the mysterious wide interval between the primary breast cancer and diagnostically confirmed metastatic tumor, which ranges from several months to dozens of years⁸. The period between primary diagnosis and gastrointestinal involvement varies from synchronous presentation to nearly 30 years; however, the reverse has also been reported occasionally, with the GI manifestation preceding a diagnosis of breast cancer^{6,7,9}. This patient developed synchronous metastasis in less than a year from the time of diagnosis.

The diagnosis of colon involvement by breast cancer metastasis is challenging; the differential could include those of benign or malignant colorectal neoplasms, an infectious and/or inflammatory process such as inflammatory bowel disease, medication/drug side effects, or even allergic gastroenteritis. Upper endoscopy and colonoscopy is use to document a mass or tumor in the lumen. GATA-3 is an integral player in breast luminal cell differentiation and has been implicated in mammary malignant transformation and carcinogenesis¹⁰. Immunohistochemistry of

GATA-3 expression is currently being utilized as a useful marker for confirming a potential mammary source, especially when facing metastatic carcinoma with an unknown origin or incomplete clinical history¹¹. In fact, immunohistochemical detection of GATA-3 protein has been proven an effective and popular tool in determining a potential breast origin, especially when dealing with metastatic high grade breast carcinoma, sarcomatoid, triple-negative breast primaries or breast carcinoma with lobular features^{10,11}. In our case, the positive labeling by GATA-3, ER and CK7 are highly consistent with a metastatic disease from a breast primary, involving multiple colonic sites in this patient. Metastasis to the gallbladder is very rare and was found only in 4.8% of cancer patients in a large study. The tumor which is most likely to metastasize to the gallbladder is gastric carcinoma and malignant melanoma¹². Metastatic breast carcinoma involving the gallbladder or biliary tract is very rare and usually presents with abdominal pain, symptoms of cholecystitis and obstructive jaundice.¹³ The patient's medical history and preoperative findings did not raise any suspicion on the possible presence of a metastatic lesion in the gallbladder. Likewise, the most common histologic classification that metastasizes to the gallbladder is that of the lobular type further making this patient indeed a rare case.

The involved mechanisms responsible for this distinctive metastatic pattern, however, remain undetermined. It has been suggested that loss of expression of the cell-cell adhesion molecule E-cadherin in ILC may contribute to the differences in metastatic patterns when compared to IDC¹⁴. Generally, breast cancer metastasis to the colon is hematogenous, although it may also result from dissemination of tumor cells by peritoneal and regional lymphatic routes. In one well aligned study, colon metastases were found in only 3% of patients (20 of 720 cases)¹⁵, which is less

frequently uncovered than upper gastrointestinal tract^{5,23}. Fewer reports described rectal metastases from breast cancer.¹⁴⁻¹⁶

CONCLUSION:

Metastatic involvement of the gastrointestinal tract secondary to breast cancer is rare. Gallbladder and colonic metastasis involving almost the entire colon from breast cancer is even rarer. Metastatic breast carcinoma involvement of the gastrointestinal tract is usually of the lobular histologic subtype. To the best of our knowledge, the case presented here is one very rarely reported in literature, showing gallbladder and pancolonic metastasis from invasive ductal breast cancer. Adequate diagnostic procedures should be performed in patients with a history of breast cancer and who show gastrointestinal symptoms to rule out the potential presence of gastrointestinal metastases.

Although rare, gastrointestinal and biliary metastasis should be considered in patients of breast carcinoma especially in cases of infiltrating lobular type. Treatment of metastatic breast cancer is generally nonsurgical, with systemic chemotherapy, biologic agents with HER2-neu positivity or anti-estrogen targeted treatment. Surgery is used for diagnosis and palliation.¹⁷

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