

Unusual Sites of Metastasis of Breast Carcinoma to Gallbladder and Colon.

Sabah Nayef Nemri¹, Nazima Haider^{2*}, Sohaila Fatima², Bouvier Francis Valere D'SA¹

¹Aseer Central Hospital, Abha 62529, Saudi Arabia

²King Khalid University, Abha, 62529, Saudi Arabia

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ABSTRACT

Breast cancer is usually associated with metastasis to lungs, bones and liver. Metastatic pattern of Infiltrating Lobular Carcinoma differs from Infiltrating Ductal Carcinoma with higher frequency of tumor extension to bone, gastrointestinal tract, genital tract, meninges and serosa. We here present two rare case reports showing this unusual pattern of metastasis of infiltrating lobular breast carcinoma to colon and gall bladder. Because of its rarity, nonspecific clinical presentation and the variable radiographic features, the diagnosis of intestinal and biliary tract metastasis by breast carcinoma is difficult.

***Corresponding author:**

Dr Nazima Haider, King Khalid University, Abha 62529, Saudi Arabia

Phone: +91 966559938735

E-mail: nazima_haider@yahoo.com



Introduction

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 lobular carcinoma (ILC) of the breast accounts for 5 to 15% of breast carcinomas and is the second most common histologic type of invasive breast cancer after invasive ductal carcinoma (IDC). Metastatic pattern of ILC differs from IDC. [1] We here present two rare case reports showing this unusual pattern of metastasis of infiltrating lobular breast carcinoma to colon and gall bladder (GB).

Case Report

CASE 1: A 73 year old Saudi female presented in Surgical emergency with complain of pain in right hypochondrium and jaundice. Blood tests showed deranged liver function tests with raised Bilirubin - 4 mg/dL (0.1 - 1.2 mg/dL), raised Alkaline phosphatase - 300 U/L (45- 115 U/L), raised Aspartate aminotransferase - 100 U/L(8- 48 U/L) and raised Alanine aminotransferase -150 U/L(7- 55U/L). Complete blood count showed increased White blood cell count - 15,000 /uL(4000- 11000/uL) and decreased Hemoglobin -10 g/dL(12- 16 g/dL). Ultrasound was done which revealed enlarged GB 12 x 3 cm with irregular thickening along with massive biliary dilatation due to ampullary stricture. Liver was normal. Common bile duct stenting was done. Later on cholecystectomy was performed and sent for histopathological examination. Whole body CT (Computerized Tomography) did not reveal any other organ involvement.

Gross examination showed an enlarged GB 11.5x 2,5 cm with irregularly thickened wall maximum thickness

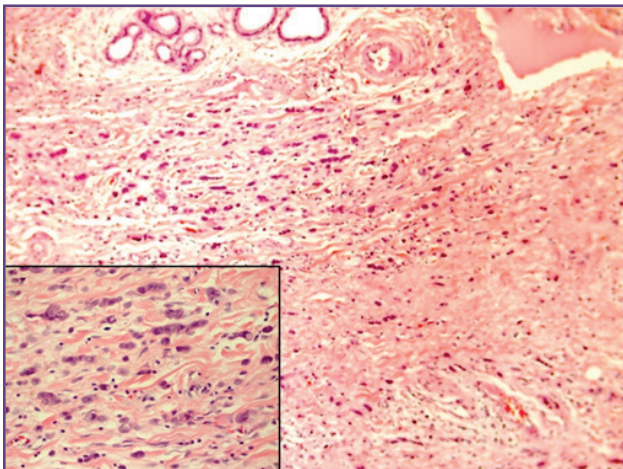


Fig. 1: Tumor cells in single file arrangement in mucosa and muscle layer of gallbladder. (Hematoxylin and Eosin, 10X and Inset, 40X)

1cm. On serosal side two attached lymph nodes were seen, 1.5x0.8cm and 3x2cm respectively.

Microscopy showed malignant cells in single file arrangement in mucosa, muscle layer and serosa of GB. **(Fig.1)** Overlying GB mucosa was normal to atrophic. Immunohistochemistry revealed these cells to be Cytokeratin(CK) CK 7 +, CK 20 -, Estrogen receptor ER+. **(Fig. 2)** Lymph nodes were positive for malignancy. A diagnosis of metastatic carcinoma to GB most likely from breast was made. She had undergone radical mastectomy 7 years ago for invasive carcinoma.

CASE 2: A 46 year old female presented to the surgical OPD (outpatient department) with complaint of pain in abdomen, nausea and alteration of bowel habits from 2 months. Ultrasound of the abdomen showed multiple colonic strictures suggestive of crohn's disease. Colonoscopy was performed confirming colonic strictures and colonoscopic biopsy was sent for histopathological examination. Microscopic examination showed patchy infiltration of lamina propria by sheets of malignant pleomorphic cells in cord like pattern. Overlying colonic mucosa was normal. **(Fig.3)** Immunohistochemistry showed them to be CK 7+, CK20-, ER + and negative for CKAE1, CD 68, TTF1. **(Fig.4)** A diagnosis of metastatic carcinoma to colon most likely from breast was made. On further clinical examination, a small mass in right breast was found with tru-cut biopsy confirming primary invasive lobular carcinoma. **(Fig.5)** Whole body CT scan did not reveal any other lesion.

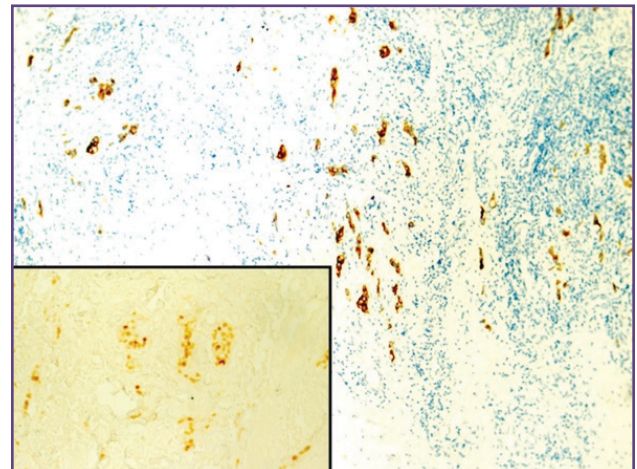


Fig. 2: Immunohistochemical study by Cytokeratin 7 and Estrogen receptor showing positivity for malignant cells. (CK 7 immunostain, 10X and Inset showing ER immunostain, 20X)

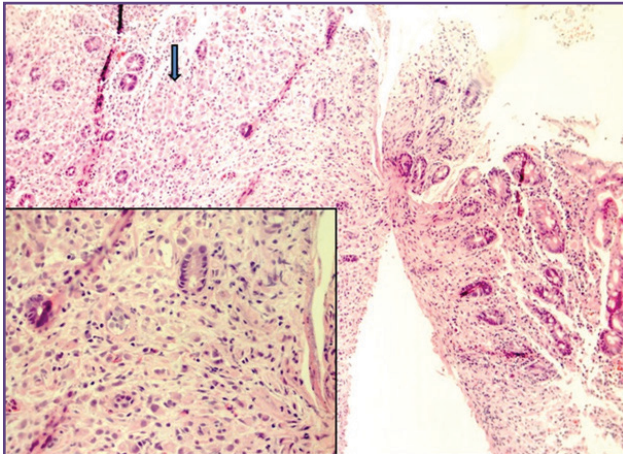


Fig. 3: Tumor cells in single file arrangement (arrow) in lamina propria with normal colonic glands. (Hematoxylin and Eosin, 10X and Inset, 40X)

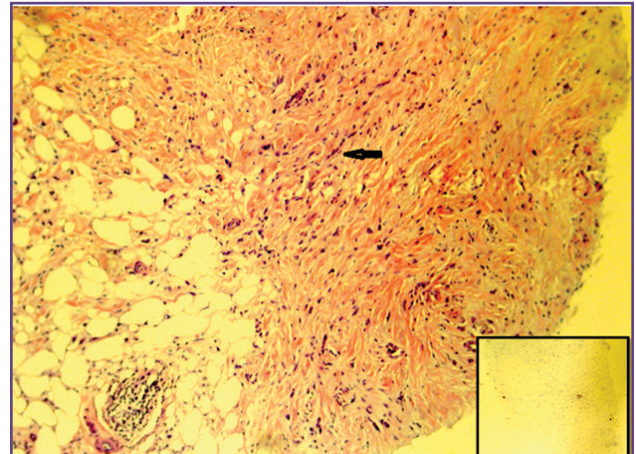


Fig. 5: Tumor cells in single file arrangement (arrow) in Trucut biopsy of right breast. (Hematoxylin and Eosin, 10X) and Inset showing E-cadherin negativity. (10X)

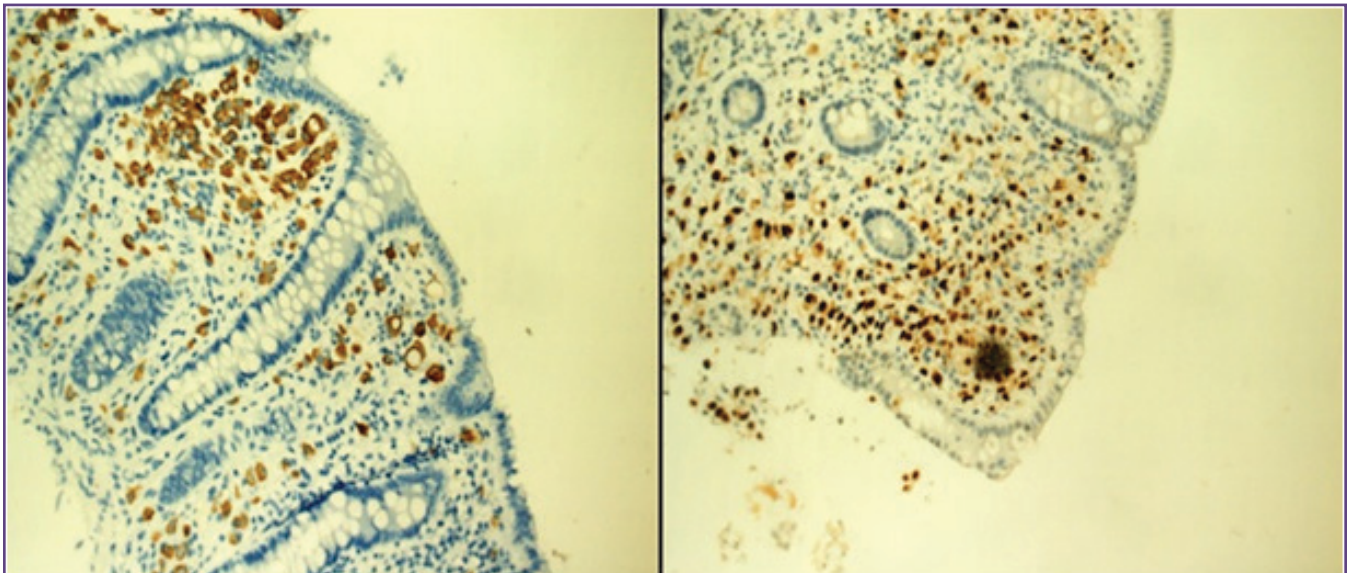


Fig. 4: Immunohistochemical study by Cytokeratin 7 and Estrogen receptor showing positivity for malignant cells. (CK7 and ER immunostain, 10X)

Discussion

Breast carcinoma is one of the most common human cancers accounting for one quarter of all female cancers. Breast cancer is usually associated with metastases to lungs, bones and liver. Invasive lobular carcinoma (ILC) of the breast accounts for 5 to 15% of breast carcinomas and is the second most common histologic type of invasive breast cancer after invasive ductal carcinoma (IDC). Metastatic pattern of ILC differs from IDC with higher frequency of tumor extension to bone, gastrointestinal tract, genital tract, meninges and serosa.^[1] Because of its rarity, nonspecific clinical presentation and the variable radiographic features,

the diagnosis of intestinal and biliary tract metastasis by breast carcinoma is difficult.^[2,3]

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 carcinoma stomach and malignant melanoma.^[4] Metastatic breast carcinoma involving the gallbladder or biliary tract is very rare and presents with abdominal pain, symptoms of cholecystitis and obstructive jaundice as seen in our case.^[5]

Gastrointestinal (GI) metastasis of breast cancer is also rare and is particularly uncommon at the time of initial diagnosis as was our case. In one study, only 1% of the patients

with breast cancer were found to have gastro-intestinal metastasis.^[6] However, the occurrence in autopsy series varied from 8% to 35%.^[7] The clinical manifestations of the majority of gastrointestinal metastases include abdominal pain, diarrhea, GI bleeding, intestinal obstruction and intussusception.^[8]

In order to differentiate primary and metastatic tumors, histopathological comparison of breast and GI specimens is essential. The morphological similarity to breast cancer and the absence of dysplasia in epithelium of intestine or gallbladder suggests a metastatic growth as was seen in our case. Primary site of disease can be found out with the help of careful history and clinical examination, histopathological examination and immuno-histochemistry.

Gallbladder and intestinal metastases of breast carcinoma are particularly linked to lobular histotype. With respect to the underlying mechanism, molecular events, such as alterations of E-cadherin expression is implicated in this rare hematogenous metastasis.^[1, 9] However, few cases of infiltrating ductal carcinoma metastasizing to gall bladder and intestine have also been reported.^[10,11,12]

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.^[13]

Conclusion

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.

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Competing Interests

None declared

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