

# Breast metastasis from recurrent gallbladder adenocarcinoma: a case report with review of the literature

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**Abstract:** Gallbladder adenocarcinoma has a poor prognostic. The leading modes of dissemination in gallbladder cancer (GBC) are lymphatic, vascular, neural, intraperitoneal, and intraductal. The most common site of dissemination is liver. Breast metastasis in GBC is an unusual site of dissemination. Only few cases have been reported in the literature. We report a rare case of solitary breast metastasis from recurrent gallbladder carcinoma in light of existing literature.

**Keywords:** Gallbladder adenocarcinoma; metastasis; breast

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## Introduction

Gallbladder cancer (GBC) is the sixth most common cancer among gastrointestinal (GI) tumors. However it is relatively rare, accounting only 2% to 4% of all malignant GI tumors (1,2).

The exact etiology of GBC is still not known. Cholelithiasis and chronic cholecystitis are the most common predisposing factors associated with GBC.

It affects predominantly women in their seventh decade of life, approximately 3-fold higher in women than in men (3).

Approximately one-third of patients with GBC present with metastasis at the time of diagnosis due to nonspecific clinical presentation which is similar to biliary colic or chronic cholecystitis and includes right upper quadrant pain, jaundice, nausea, vomiting, anorexia, and weight loss (4-6).

The leading modes of dissemination in GBC are lymphatic, vascular, neural, intraperitoneal, and intraductal (7).

The most common site of dissemination is liver (8,9). Breast metastasis in GBC is an unusual site of dissemination. Only few cases have been reported in the literature (10-12).

GBC is an aggressive tumor and carries a poor prognosis with 5-year survival rate less than 10% (3,13).

We report a rare case of solitary breast metastasis

from recurrent gallbladder carcinoma in light of existing literature.

## Case representation

A 68-year-old woman underwent laparotomic cholecystectomy for an adenocarcinoma of the gallbladder approximately 10 months ago in a local hospital. She did not receive any adjuvant treatment.

Eight months later, she presented with a subcostal mass at the abdominal surgical scar progressively increasing in size. The biopsy with histopathological and immunohistochemical examination showed moderately differentiated metastatic adenocarcinoma. Tumor cells were intensely positive for the antibody anti-CK7 and weakly for anti-CK20, suggesting gallbladder adenocarcinoma as primary tumor. The patient was referred to our hospital for further management.

Whole-body computed tomography (CT) demonstrated no evidence of distant metastasis. She underwent wide local excision and exploratory laparotomy. No further treatment was indicated on multidisciplinary meeting.



**Figure 1** The breast nodule in the upper outer quadrant of the right breast.

At the ninth month after surgery, surveillance follow-up CT scan revealed a heterogeneous suspect nodule at the upper outer quadrant of right breast with no distance metastasis.

Physical examination confirmed a 5 cm sized, irregular shaped, and firm nodule at her right breast located at the junction of upper outer quadrant and the axillary tail (*Figure 1*).

Bone scan, tumor markers including CA19-9, carcinoembryonic antigen (CEA), CA15.3, and routine blood tests, were normal.

Needle core biopsy of the breast nodule revealed metastasis of moderately differentiated adenocarcinoma. Immunohistochemistry showed positive reaction for CK7, CK19 and negative reaction for CK20 and estrogen and progesterone receptors, this immunohistochemistry was compatible with metastatic gallbladder carcinoma.

The patient underwent combined chemotherapy based on gemcitabine and cisplatin and planned for further surgery if there will not have a progression disease. She has received two cycles of chemotherapy till date with clinical response.

## Discussion

GBC is the sixth most common cancer among GI tumors and the most common cancer of the biliary tract. However this malignancy is relatively rare, accounting only 2% to 4% of all malignant GI tumors (1,2).

Moreover, the incidence of GBC varies significantly based on geographic region and ethnicity. GBC is particularly higher in South American Countries like Chile and Bolivia and some Asian countries like some northern India, Pakistan and Japan (2,14). This variance suggests that both environmental exposure and genetic factors could be

involved in carcinogenesis (1).

Although the exact etiology of GBC is still not known, cholelithiasis and chronic cholecystitis are the most common predisposing factors associated with GBC; 75% of patients with GCB have gallstones and a history of cholelithiasis leads to 4- to 5-fold higher risk of developing GBC than patients without cholelithiasis (5).

GBC is more prevalent in women, approximately 3-fold higher in women than in men, it occurs in their seventh decade of life (3).

Clinical presentation of GBC is not specific; it is similar to biliary colic or chronic cholecystitis, and 0.5–1.5% of GBC is diagnosed incidentally after simple cholecystectomy for presumed gallbladder stone disease. Common symptoms include usually right upper quadrant pain, jaundice, nausea, vomiting, anorexia, and weight loss (4-6,15-17).

Transabdominal ultrasound is usually the initial modality in diagnosing the disease and CT is often used for staging the disease (4).

GBC is an aggressive tumor. At the time of the diagnostic, only 10% of patients have resectable tumors and one-third of all patients present with metastasis. GBC has a poor prognosis with 5-year survival rate less than 10% (3,13). Our patient presented initially with local disease without metastasis and in spite of recurrence in abdominal scar then breast metastasis, our patient is alive and well 26 months following her initial diagnosis.

The leading modes of dissemination in GBC are lymphatic, vascular, neural, intraperitoneal, and intraductal (7).

The most common sites of dissemination are liver, regional lymph nodes; and peritoneum (7-9).

Extra abdominal metastasis involves mostly lungs (9,12,18). Rare sites of metastasis have been reported including bone, brain, skin, orbit, and heart (9,19-27).

Only 0.5% to 6.6% from all breast malignancies is metastasis (28). The most common primary tumors with metastases to breast are lymphoma, melanoma, rhabdomyosarcoma, lung tumors, and ovarian malignancies (28,29). Breast metastasis from gallbladder carcinoma is extremely rare. To date only few case reports have been reported in the literature (11,12,30). Therefore it brings up the problem of diagnostic and treatment. There is no consensus for its management, generally palliative chemotherapy is used. However in exceptional cases when the tumor shows good biological behavior, curative approach can be offered.

In our case, regarding the over survival of 26 months following the initial diagnosis and the occurrence of second

unique site of recurrence, chemotherapy was offered and further surgery is planned if there will not have a progression disease.

## Conclusions

In conclusion, this case illustrates a rare case of breast metastasis from gallbladder adenocarcinoma which is an unusual site of dissemination and only limited cases have been reported in the literature. Clinicians and histopathologists should though keep vigilance in cases of breast nodule in patients with gallbladder carcinoma in order to set the diagnostic and improve the survival period.

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## Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

*Informed Consent:* Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

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