

# Patient with metastatic breast cancer presenting as acute cholecystitis with one-year survival on hormonotherapy

**Authors' Contribution:**  
A – Study Design  
B – Data Collection  
C – Statistical Analysis  
D – Data Interpretation  
E – Manuscript Preparation  
F – Literature Search  
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## ABSTRACT:

Breast cancer has high metastatic potential with distant metastases involving mainly lungs, liver and bones. Less frequently it gives distant spread to other organs. Herein we would like to present a very rare case of an acute cholecystitis which turned out to be a metastatic breast cancer in previously healthy woman. A female patient, 64-years old, presented to the emergency department with symptoms of biliary colic and acute abdomen. During the emergency cholecystectomy, we diagnosed the gallbladder empyema with thickened wall. There were also multiple metastatic nodules in the peritoneal cavity and an excessive amount of free fluid. The emergency physicians diagnosing female patient with the acute abdominal symptoms and a breast cancer history might suspect malignant spread into abdominal organs including gallbladder. On the other hand, acute cholecystitis symptoms might be the first symptoms of metastatic process in the gallbladder from the unknown primary source, which may be breast.

## KEYWORDS:

breast neoplasm, advanced cancer, metastatic disease, Acute cholecystitis, gallbladder, laparoscopic cholecystectomy

## INTRODUCTION

Cholecystitis is the second most frequent cause of emergency surgical interventions. Symptoms, signs, laboratory tests, and additional examinations like abdominal ultrasound scan allow to make the diagnosis of acute cholecystitis in the majority of cases. Treatment options for cholecystitis include conservative approach, open surgery, and laparoscopic cholecystectomy performed in the majority of patients. After resection, the gallbladder should be sent for histopathology to exclude cancer. In up to 6% of cases, gallbladder cancer can be metastatic [1,5-9], most frequently secondary to stomach, lower gastrointestinal tract, liver, kidney, or skin (malignant melanoma) cancer [1,4-9]. Breast cancer, the most frequent cancer in women, has a very high metastatic potential, and it metastasizes mainly to the lungs, liver, and bones. Less frequently, it spreads to the central nervous system, pericardium, gastrointestinal tract, ovaries, or peritoneum [2-6].

To our knowledge, only few cases of breast cancer with gallbladder metastases have been described, mainly in patients already diagnosed with breast cancer. Moreover, in only 3 reports, did acute cholecystitis precede the diagnosis of breast cancer, which was based on histopathological analysis of gallbladder samples [2,9]. In this case report, we describe a patient who presented with acute cholecystitis symptoms due to metastatic lobular breast carcinoma.

## PATIENT PRESENTATION

A 64-year-old female patient presented to our emergency department due to worsening biliary colic symptoms for six months. Two days earlier, the symptoms became severe, and were localized in the right hypochondriac area. The patient complained of loss of appetite, nausea, and vomiting. She reported involuntary weight

loss of 5 kilograms over the past 6 months. Except for first-degree arterial hypertension, the medical and surgical history were unremarkable. Blood tests (CRP, white blood cell count, bilirubin) were normal, and an abdominal ultrasound showed changes suggestive of acute cholecystitis. Due to symptoms of "acute abdomen", the patient was qualified for emergency cholecystectomy.

## SURGICAL PROCEDURE

As per our local protocol, diagnostic laparoscopy with typical three-port cholecystectomy was performed. Gallbladder empyema was diagnosed intraoperatively. During laparoscopy, we found an excessive amount of free fluid in the peritoneal cavity and multiple small nodules along both stomach curves, in the lesser and major omental sacs, small intestine mesentery, and parietal peritoneum. An incisional biopsy of selected nodules and aspiration of free fluid for cytology were performed. After gallbladder dissection, we found pus with no gallstones or other obvious abnormalities. A meticulous abdominal inspection showed no primary cancer in the abdominal cavity despite obvious metastatic changes in the peritoneum.

## DIAGNOSTIC WORKUP

When the patient recovered after surgery, we searched for the primary cancer focus.

Expect for elevated Ca125 (160 units/mL), the laboratory tests were normal. Chest x-ray and abdominal ultrasound were normal. Abdominal computed tomography showed multiple metastatic foci, up to 30mm in diameter, in the same locations as during laparoscopy. It also showed metastatic infiltration of the stomach and pancreas, with the 'omental cake' appearance.

Subsequently, we performed gastroscopy, which showed an ulceration in the stomach's trunk; thus, biopsies were taken. Finally, mammography and bilateral breast ultrasound showed multifocal, bilateral breast tumors with bilateral nodal involvement.

Cytology confirmed the presence of tumor cells (adenocarcinoma) in the free fluid sampled from the abdominal cavity. On histopathology, the gallbladder and peritoneal nodules were infiltrated by metastatic lobular breast carcinoma. Gastric biopsies showed poorly differentiated adenocarcinoma, most probably of a mammary origin.

Based on the above-mentioned findings, we made a final diagnosis of metastatic, invasive lobular breast carcinoma (G2); the estrogen receptor (ER) was found in 99% of cells, the progesterone receptor (PR) was absent, the HER2 status was negative, and 20% of cells were positive for Ki67.

Because the disease was advanced, with multiorgan metastases, we started tamoxifen treatment with proton pump inhibitors due to the gastric mucosa changes found. The patient was discharged home after treatment initiation, with regular outpatient follow-up visits every 3 months. On control mammography, six months after the surgery, clinical partial regression was seen. An ultrasound examination of the lymphatic drainage showed a high degree of regression. At 12 months, CT and breast ultrasound showed further partial regression of the primary disease with a significant reduction of the lymphatic involvement and regression of the peritoneal disease. To date, no new foci of the disease have been found. Over the last year, the patient has reported only minor, occasional, upper abdominal pain (visual analogue score of 2-3 points); she has had good appetite and stable weight. The most recent performance score was PS=0. The patient still receives hormonal therapy for disseminated breast cancer, and attends follow-up visits and radiology tests every 3 months.

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## DISCUSSION

Invasive lobular breast carcinoma is the second most frequent histological type of breast tumors [4]. In around 60% of newly diagnosed patients with lobular breast carcinoma, there are lymphatic or distant metastases present at the time of diagnosis [4,6]. However, only a few reports have described breast cancer metastases to the gallbladder [3]. Khan et al. reviewed 13 cases of breast cancer metastases to the gallbladder, including 8 cases with lobular breast carcinoma, 3 with ductal breast carcinoma, and 2 with unknown types invasive breast carcinoma [3]. Invasive lobular breast carcinoma, unlike ductal breast carcinoma, tends to metastasize to the gastrointestinal tract, the reproductive system, and the peritoneum [2,3]. Similar to our patient, 7 out of 13 patients described by Khan et al. survived at least one year [3]. Notably, in all these patients, gallbladder metastases were found during treatment for breast carcinoma, which indicated disease dissemination. In our case, acute cholecystitis symptoms preceded the diagnosis of cancer despite advanced disease with multiorgan metastases. In such cases, treatment choice is difficult and limited. Before the diagnosis, the patient was in good condition, with good performance status, and ECOG PS score of 0. Due to disseminated, multifocal, bilateral breast cancer [cT1N1M1, histologically luminal B (HER2 negative, ER positive, PR negative, Ki67 in 20% of cells)], surgical treatment was contraindicated. Based on radiological examinations that showed extensive clinical regression, a multidisciplinary team decided that hormonal treatment would be the most suitable treatment option for the patient.

## CONCLUSIONS

Emergency physicians who treat female patients with acute abdominal symptoms and a history of breast cancer should suspect metastatic involvement in the abdominal organs, including the gallbladder. Also, acute cholecystitis symptoms might be the initial symptoms of metastatic disease of an unknown primary source, including the breast.

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