ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 17, Issue 12, 2024

Online - 2455-3891
Print - 0974-2441

Case Report

ATYPICAL PRESENTATION OF METASTATIC LOBULAR BREAST NEOPLASM

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Received: 20 August 2024, Revised and Accepted: 10 October 2024

ABSTRACT

The diagnosis of cholecystitis is based on physical examination, laboratory tests, and abdominal ultrasound. After cholecystectomy, the surgical specimen is sent to the pathology department for routine histopathological examination to rule out pre-malignant and malignant conditions. Even less common is metastatic breast cancer that has spread to the gallbladder, which is itself a rare occurrence. We present a case of a 55-year-old female patient who underwent cholecystectomy for symptomatic chronic calculous cholecystitis. On histological examination, to the utmost surprise, a metastatic deposit in the wall of the gallbladder was detected by the pathologist, with a specific pattern of cell disposition, pointing to the primary site to be the breast, of which the patient was totally unaware. Metastasis in the gallbladder from primary lobular carcinoma of the breast was confirmed by a Tru-Cut biopsy from an ill-defined right breast lesion, with immunohistochemistry showing positive E-cadherin staining. Symptoms of right hypochondrial pain with nausea and vomiting in a patient should be investigated meticulously, as it can ultimately lead to the diagnosis of primary breast cancer. The role of the pathologist is emphasized in tracing the primary source of cancer and arriving at a clinical diagnosis.

Keywords: Cholecystitis, Cholecystectomy, Gallbladder, Metastasis, Breast cancer, Indian file.

 DOI: http://dx.doi.org/10.22159/ajpcr.2024v17i12.52399. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

INTRODUCTION

Worldwide, breast cancer affects more women than any other type of cancer. It is typically associated with metastases to bone, lung, lymph nodes, liver, and brain [1]. However, metastasis to the gallbladder from breast cancer is extremely rare, with only 15–20 cases reported in the literature [2]. The histological type of breast cancer can influence the pattern of metastasis. In particular, lobular carcinoma is known for its propensity to metastasize to unusual sites, including the gastrointestinal tract, peritoneum, and retroperitoneum [3].

The rarity of gallbladder metastasis from breast cancer can be illustrated by various studies. For instance, Chan reported in a series of 7910 cholecystectomy specimens that only 36 cases (0.455%) of metastatic carcinoma were found [4]. These metastases were more commonly secondary to cancers of the stomach, lower gastrointestinal tract, liver, kidney, or skin (specifically malignant melanoma). Similarly, Murguia *et al*. demonstrated that metastasis to the gallbladder accounts for 3.1% of incidental gallbladder malignancies detected during routine pathological examination, with metastasis from breast cancer being even rarer [5].

Here, we present a case in which metastatic deposits in the gallbladder wall provided a critical clue to the primary site of breast carcinoma. This case underscores the essential role of the pathologist in meticulously screening each slide, highlighting the breakthrough in pathology that can arise from such detailed examination.

CASE HISTORY

A 55-year-old female presented with dull right upper abdominal pain that had been gradually worsening over the past few weeks. Symptoms of the pain included an upset stomach, vomiting on occasion, gas, and flatulence. No changes in her bowel habits, weight loss, or fever were reported by her. There were no visible masses or symptoms of acute abdomen; nevertheless, there was some softness and slight soreness in the right upper quadrant of the belly. She exhibited steady vital signs.

Investigations

To evaluate her symptoms, a series of investigations were conducted as follows

Imaging studies

Both plain and contrast-enhanced magnetic resonance cholangiopancreatography revealed a diffusely thickened and contracted gallbladder containing a 16 mm-sized T2 hypointense calculus. The imaging findings were consistent with chronic calculous cholecystitis.

Ultrasonography (USG) of the whole abdomen showed a grossly contracted gallbladder with a lumen containing a solitary 16 mm-sized calculus. These findings were suggestive of chronic calculous cholecystitis. No other significant abnormalities were noted in the liver, bile ducts, pancreas, or other abdominal organs.

Laboratory tests

Liver function tests:

- Serum glutamic oxaloacetic transaminase: 108 U/L (normal range: 0–35 U/L)
- Serum glutamic pyruvic transaminase: 103 U/L (normal range: 0–35 U/L)
- Alkaline phosphatase: 476 U/L (normal range: 44–147 U/L)
- Total bilirubin: 1.19 mg/dL (normal range: 0.1–1.2 mg/dL)

Complete blood count, serum electrolytes, and renal function tests were within normal limits.

Management

The patient underwent a laparoscopic cholecystectomy to address her gallbladder condition.

Gross/macroscopy

On examination, the gallbladder specimen, measuring 2 cm × 1 cm × 0.8 cm, revealed a velvety mucosa that was largely lost (Fig. 1). The wall thickness was noted to be 0.3 cm. A solitary calculus was also identified.

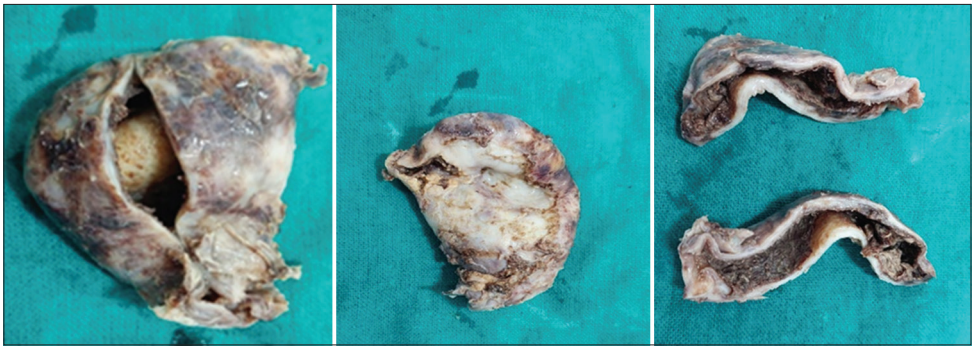

Fig. 1: Gall bladder gross image

Microscopy
Microscopic analysis revealed several significant findings, including foci of denudation of the gallbladder mucosa, hypertrophy of the muscular wall with thickened nerve bundles, formation of Rokitansky–Aschoff sinuses, surrounding stromal fibrosis, and mild infiltration of chronic inflammatory cells.

Importantly, the serosal and muscular layers were infiltrated by malignant cells arranged in an Indian file pattern (Fig. 2). These cells exhibited scanty eosinophilic cytoplasm, high nuclear-cytoplasmic ratio, and hyperchromatic irregular nuclei. These histological features suggested metastatic deposits, likely from lobular carcinoma of the breast, alongside features of chronic cholecystitis in the remaining gallbladder wall.

Radiological evaluation of breast
Radiological imaging, including USG, revealed a defined soft-tissue lesion located at the 11–12 o'clock periareolar region of the right breast, accompanied by prominent right axillary lymph nodes (Fig. 4). This finding was classified as USG BIRADS category 4c, indicating a high suspicion of malignancy. The left breast appeared to have a normal architecture. Based on these findings, an urgent fine needle aspiration cytology or Tru-Cut biopsy was recommended.

Tru-cut biopsy
The biopsy results were striking, showing malignant cell infiltration in an Indian file pattern within the breast tissue (Fig. 3). In addition, a targetoid arrangement of cells around ducts and hyalinized vessels was observed, along with areas of necrosis and hemorrhage. These features were consistent with lobular carcinoma of the breast.

Immunohistochemistry (IHC)
IHC confirmed the diagnosis, showing loss of e-cadherin staining, thereby corroborating the presence of metastatic deposits in the gallbladder originating from primary lobular carcinoma of the right breast.

DISCUSSION

This case emphasizes the critical role of thorough pathological examination in uncovering rare metastatic presentations, ultimately guiding the appropriate clinical management.

The gallbladder is an uncommon site for metastasis, with tumors such as malignant melanoma being more common, occurring in 15% of cases. Other less common primary sites include renal cell cancer, lung cancer, and cervical cancer. Breast carcinoma metastasizing to the gallbladder is extremely rare. Invasive lobular cancers of the breast often show a preference for metastasizing to the peritoneum, retroperitoneum, and gastrointestinal tract, with only a few cases of metastasis to the gallbladder published to date [6].

The rarity of gallbladder metastasis from breast cancer makes this case particularly noteworthy. The metastatic pathway of lobular carcinoma to the gallbladder is not well understood but is thought to involve

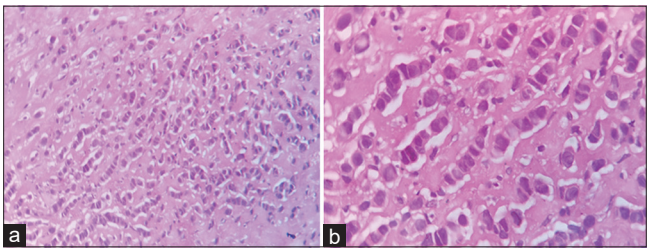

Fig. 2: Gallbladder microscopy images, (a) gallbladder tissue – Indian file pattern (×20), (b) gallbladder tissue – Indian file pattern (×40)

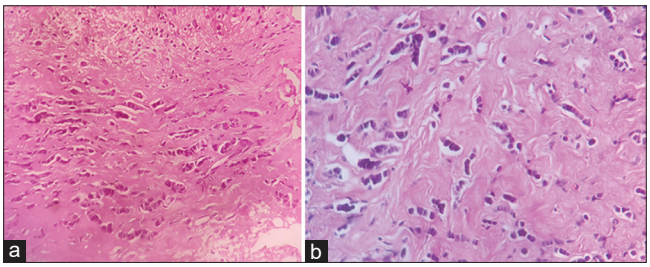

Fig. 3: Breast tissue microscopy images, (a) breast tissue (×20), (b) breast tissue (×40)

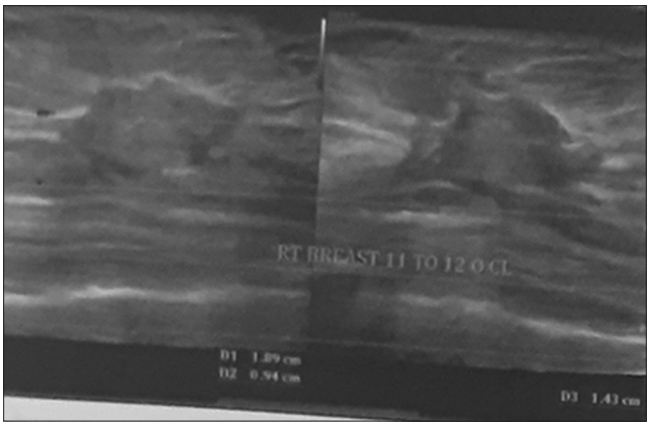

Fig. 4: Ultrasonography of breast

hematogenous spread. Metastatic disease should be considered in patients exhibiting unusual symptoms or when standard diagnostic results fail to provide a complete picture, as demonstrated in this example [7].

The role of the pathologist is crucial in identifying such rare occurrences. In this case, the meticulous histopathological examination revealed the unexpected metastatic breast carcinoma, which would otherwise

have gone undetected. The identification of metastatic cells in the gallbladder led to further investigation, which ultimately diagnosed the primary breast carcinoma, underscoring the importance of a thorough pathological examination.

Furthermore, the use of IHC played a vital role in confirming the diagnosis. Loss of e-cadherin expression is characteristic of lobular breast carcinoma, helping differentiate it from other types of invasive breast cancer [8]. This case exemplifies the need for comprehensive diagnostic workups, including advanced imaging and histopathological techniques, to uncover the primary source of metastasis.

CONCLUSION

Metastatic gallbladder involvement is rare, especially in the case of primary breast carcinoma, and usually manifests with abdominal pain mimicking acute or chronic cholecystitis. Gallbladder metastasis detected by the pathologist consequently led to the detection of the primary source of the malignancy in the breast. Each case of acute/chronic cholecystitis or right hypochondrial pain with nausea/vomiting in a patient should be screened thoroughly to detect metastatic gallbladder disease, which must be treated properly due to its poor prognosis.

The role of a pathologist is extremely vital in the proper diagnostic evaluation of not only the primary pathology of the organ but also any associated pathology. In the case of metastasis, pathological evaluation can provide a clue about the primary site, emphasizing the importance of tracing the primary source of cancer and arriving at a clinical diagnosis.

AUTHOR'S CONTRIBUTION

Nil.

INFORMED CONSENT

Written informed consent was obtained from the patient for her anonymized information to be published in this article.

CONFLICT OF INTEREST

Nil.

AUTHORS FUNDING

Nil.

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