

CASE REPORT

Gallbladder metastasis from occult lobular breast carcinoma: A case report

Mirsad Dorić¹, Nina Čamdžić^{1*}, Dževad Durmišević², Mirsad Babić¹, Edina Lazović Salčin¹, Suada Kuskunović-Vlahovljak¹

1. Department of Pathology, Faculty of Medicine, University of Sarajevo, Bosnia and Herzegovina

2. Department of Pathology, Cantonal Hospital "Dr. Irfan Ljubijankić", Bihać, Bosnia and Herzegovina

Introduction: Bones, lungs, brain and liver are the most common metastatic sites of breast carcinoma, although invasive lobular carcinoma can give metastases to less common sites, such as the gastrointestinal tract and the female genital tract. **Case presentation:** We present the case of a 57-year-old female with colic abdominal pain that was sent to surgery for cholecystectomy. Histopathology revealed a poorly cohesive individual or in single file neoplastic cells infiltrating all layers of the gallbladder. Immunohistochemistry revealed these cells to be CK 116, CK7, GCDPF-15, ER and PR positive, and CK20, HER-2, S-100 and E-cadherin negative. PET/CT showed numerous lytic bone lesions, but ultrasound, mammography, MRI and PET/CT revealed no breast mass. **Conclusion:** Although rare and poorly understood, metastases of invasive lobular carcinoma to gallbladder do exist in a minor percentage of patients, presenting usually as exacerbated cholecystitis. The problem are silent cases and patients with no history of breast carcinoma. This case is unique in that even after the diagnosis of metastatic lobular breast carcinoma to the gallbladder, the primary tumour of the breast was not detected.

Keywords: lobular carcinoma, breast, metastasis, gallbladder

Received 14 June 2023 / Accepted 3 October 2023

Introduction

Invasive lobular carcinoma (ILC) is the second most common histologic type of breast carcinoma, accounting for 5-15% of cases. The metastatic pattern of ILC differs from invasive ductal carcinoma (IDC) and affects not only the most common metastatic sites like bones, lungs, brain and liver, but also the gastrointestinal (GI) tract, peritoneum and uterus [1]. Metastases to gallbladder are rare, affecting less than 5% of patients with breast carcinoma [2,3].

Here we report a case of incidental metastatic lobular carcinoma of the breast to gallbladder with unusual clinical and radiologic presentation.

Case presentation

A 57-year-old female was admitted to the hospital due to vomiting and colic pain in the upper right abdominal quadrant with a more than one month history of constant burping and periodic nausea. Abdominal ultrasound (US) showed the presence of gallstones with a thickened wall of the gallbladder. The patient was admitted to surgery for cholecystectomy. In history, patient had no chronic diseases. Previously, she had cranial meningioma which was surgically removed 15 years ago.

Gross examination showed a gallbladder measuring 5,5x 2,5 cm with an irregularly thickened wall up to 10 mm, with normal to atrophic overlying mucosa. Histopathology revealed signs of chronic cholecystitis and focal cholesterosis. All layers of the gallbladder, from mucosa to serosa, were infiltrated by poorly cohesive individually dispersed neoplastic cells or arranged in a thin single file pattern (Figure 1).

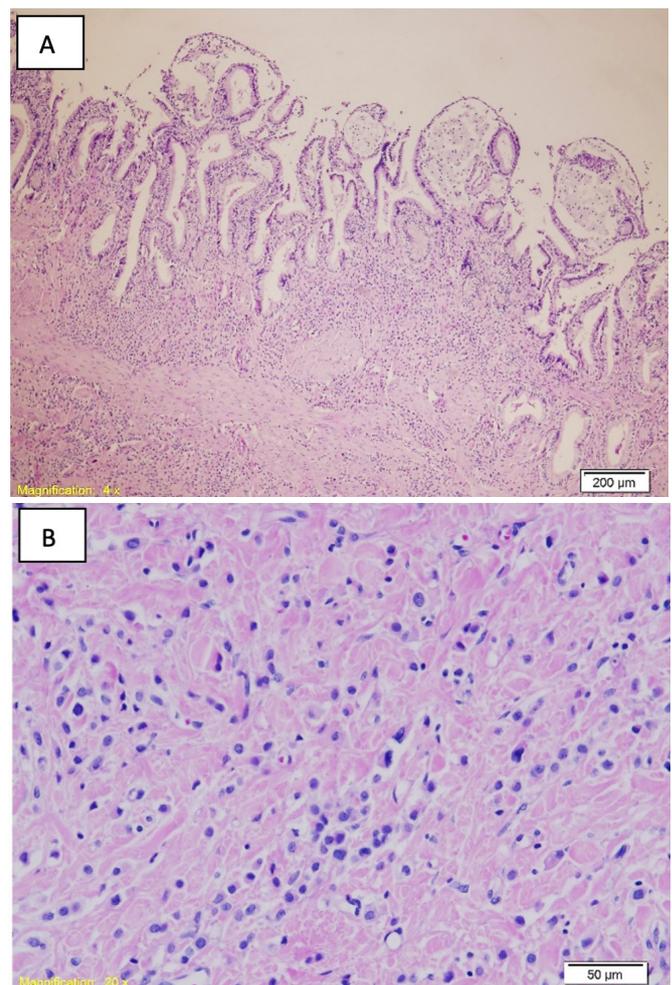


Fig. 1. Tumour is composed of non-cohesive cells that are individually dispersed or arranged in a single file pattern (H&E: A) x40; B) x200).

* Correspondence to: Nina Čamdžić
E-mail: nina.camdzic@mf.unsa.ba

Immunohistochemistry revealed these cells to be CK 116, CK7, GCDFP-15, ER and PR positive, and CK20, HER-2, S-100, E-cadherin negative (Figure 2).

The pathologic report was consistent with metastatic lobular carcinoma of the breast. The patient denied a family history of breast cancer. Mammography revealed no pathologic changes in breast tissue. It showed discrete signs of fibrocystic change. Axillary lymph nodes showed post-inflammatory changes. Ultrasound and magnetic resonance

imaging (MRI) of the breast (conducted two months apart, after the cholecystectomy), revealed no suspect pathologic mass. Right-sided axillary lymph nodes were only slightly enlarged, with unclear aetiology, most probably indicative for reactive changes. The fine needle aspiration cytology of lymph nodes was recommended. Since there was no obvious breast lesion, the biopsy was sent for a second opinion to another institution. The diagnosis of metastatic lobular carcinoma was confirmed. Positron emission tomography

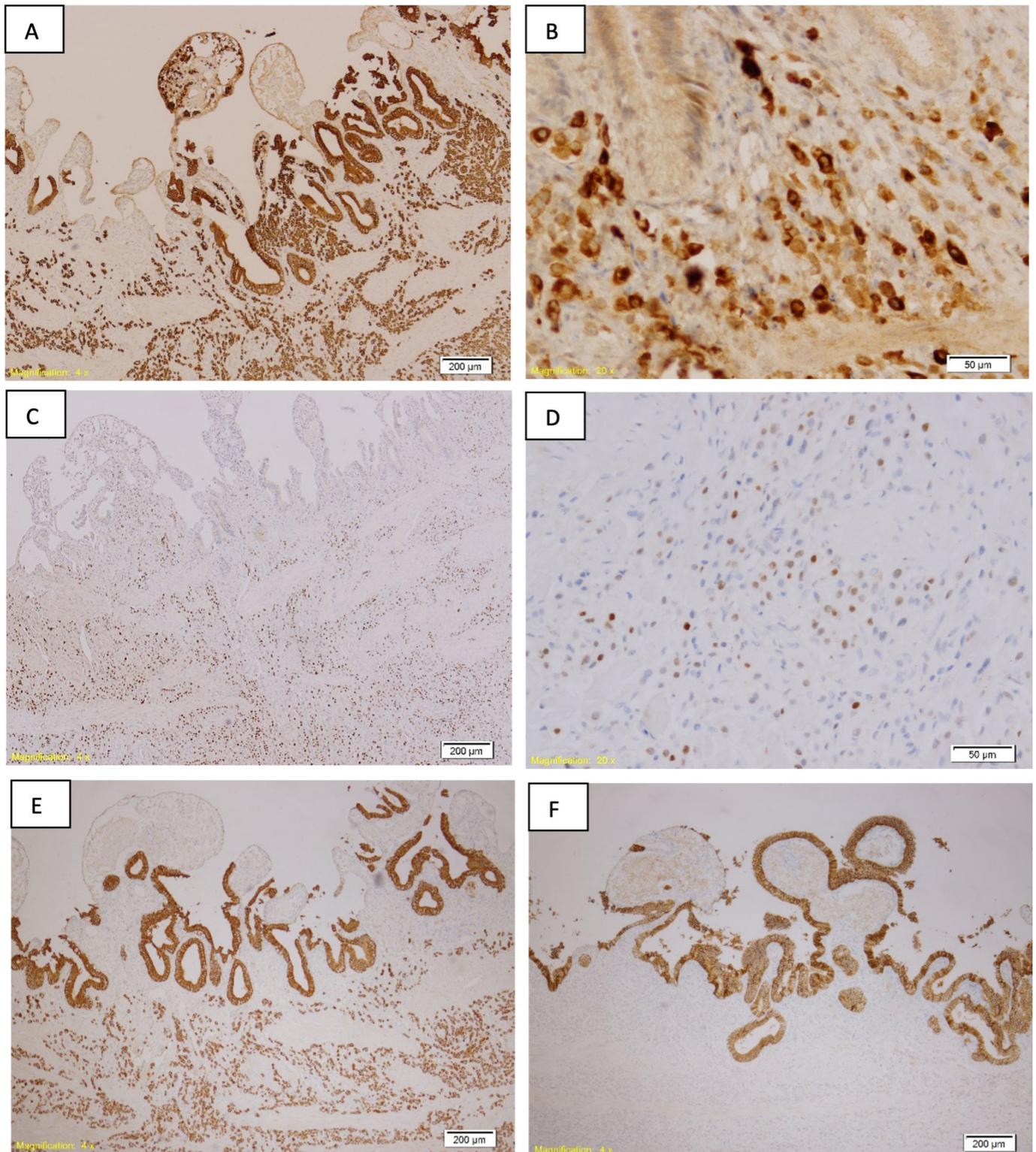


Fig. 2. Immunohistochemistry showed positivity of tumour cells for: A) CK7, x40; B) GCDFP-15, x200; C) ER, x40; D) PR, x200; E) CK116, x40; while tumour cells were E-cadherin negative F) E-cadherin, x40.

(PET)/computed tomography (CT) with 2-deoxy-2-[18F] fluoro-D-glucose (18F-FDG) showed numerous lytic bone lesions affecting the thoracic and lumbar spine, sacrum, ileum and sacroiliac joints. It also showed a few hyperdense lymph nodes of the right axilla and behind the lateral contour of the right pectoral muscle, but without significant focus of increased FDG-18 accumulation. Postoperative MRI of the abdomen showed free fluid accumulation and irregular thickening of the stomach in antral region, together with peritoneal carcinosis. The patient was sent to Oncology council for treatment options, but later was lost to follow-up. Searching the hospital's archives, we found out that the patient died due to metastatic disease very soon after the establishment of the diagnosis.

Discussion

Lobular carcinoma of the breast usually presents as vague findings including thickening, induration or poorly defined breast mass. It is generally diagnosed at a more advanced stage compared to invasive breast carcinoma of no special type [4,5].

Metastases to the gallbladder are relatively rare, with a frequency of 2-5%, according to autopsy findings [2,3]. The most common metastases to the gallbladder are from gastrointestinal malignancies, including gastric, colorectal and pancreatic carcinoma, melanoma, renal cell carcinoma and breast carcinoma [6]. According to literature and population cohorts, breast cancer is the most frequent primary origin of gallbladder metastasis in the female population. The most common histological types of primary breast cancer found as metastases in the gallbladder are invasive ductal carcinoma/adenocarcinoma not otherwise specified (NOS) and invasive lobular carcinoma [6]. The majority of gallbladder metastasis is diagnosed as metachronous, usually more than six months after the primary tumour diagnosis. There are several case reports of metastatic breast cancer to the gallbladder found incidentally on elective cholecystectomy for biliary symptoms. However, most of these cases had a known history of breast cancer [7,8]. According to literature, there are 24 cases described, with the majority of patients already being diagnosed of primary breast carcinoma [7, 9, 10]. There are only three described cases of incidental metastatic lobular carcinoma to the gallbladder without a previous history of primary breast carcinoma [7, 9, 11]. Since our presented case has no history, nor clinical and radiologic findings of an existing tumour in the breast, but has confirmed a histopathologic diagnosis as metastatic breast cancer in the gallbladder, we could not clearly classify this tumour as metastatic cancer of unknown primary (CUP). CUP is defined as a tumour in which the organ of origin cannot be reliably determined by combining clinical (including imaging and endoscopy) and histopathological (including classical immunohistochemical biomarkers) evaluations [12]. We could rather classify this case as occult breast cancer (OBC), which is defined as a clinically recognizable metastatic carcinoma

from an undetectable primary breast tumour [13]. It accounts for 0.3–1% of all breast cancers with metastasis to lymph nodes, followed by the liver, bone, and skin as the first presentation of the disease [13]. In the presented case, even after the diagnosis of metastatic lobular carcinoma, none of the radiologic imaging methods detected breast mass. Only lymph nodes of right axilla were increased in density, but of uncertain aetiology. The proposed fine needle aspiration cytology of the enlarged lymph nodes was never conducted, since the patient was lost to follow-up.

Clinical presentation in this case was similar to CUPs - severe and rapidly worsening metastasis-related symptoms [12]. The prognosis for occult breast cancer that presents as metastatic disease is considered very poor, with a 2-year survival rate of 20%. Treatment options are based on its clinical presentation and on its histological and immunohistochemical evaluation [13]. Treatment of previously described cases of metastatic breast carcinoma to gallbladder was the treatment of metastatic breast cancer disease [7, 9, 10].

Conclusion

Although rare and poorly understood, metastases of invasive lobular carcinoma to gallbladder do exist in a minor percentage and should be considered in patients with a history of primary breast carcinoma, especially in case of exacerbated cholecystitis. The problem are silent cases and patients with no history of breast carcinoma. This case is unique in that even after the diagnosis of metastatic lobular breast carcinoma to the gallbladder, the primary tumour of the breast was not detected. The primary breast cancer remained clinically and radiologically occult; however, histological and immunohistochemical findings were fundamental to identify its origin. To our best knowledge, this is the first described case in our country.

Author's Contributions

All authors participated in the design, interpretation of the studies and analysis of the data and review of the manuscript; MD (Conceptualization, Writing – original draft, Data curation, Methodology, Project administration, Resources); NČ (Conceptualization, Writing – original draft, Supervision, Validation, Visualization); DžD (Investigation, Resources, Conceptualization); MB (Investigation, Methodology, Supervision); ELS (Supervision, Validation, Writing – review & editing); SK-V (Supervision, Validation, Visualization, Writing – review & editing).

Conflict of interest

None to declare.

References

1. Mamtani A, King TA. Lobular Breast Cancer: Different Disease, Different Algorithms? *Surg Oncol Clin N Am*. 2018; 27(1):81-94.
2. Disibio G, French SW. Metastatic patterns of cancers: results from a large autopsy study. *Arch Pathol Lab Med*. 2008; 132(6):931-9.
3. Abrams HL, Spiro R, Goldstein N. Metastases in carcinoma; analysis of

- 1000 autopsied cases. *Cancer*. 1950; 3(1):74-85.
4. Li CI, Uribe DJ, Daling JR. Clinical characteristics of different histologic types of breast cancer. *Br J Cancer*. 2005; 93(9):1046-52.
 5. Dedes KJ, Fink D. Clinical presentation and surgical management of invasive lobular carcinoma of the breast. *Breast Dis*. 2008-2009; 30:31-7.
 6. de Bitter TJJ, Trapman DM, Simmer F, et al. Metastasis in the gallbladder: does literature reflect reality? *Virchows Arch*. 2022;480(6):1201-1209.
 7. Magalhães JS, Matos L, Santos T, Nora M. Elective cholecystectomy as a rare presentation of metastatic breast cancer. *J Surg Case Rep*. 2018; 2018(11):rjy301.
 8. Riaz N, Ahmed R, Afzal S, Masood N. Breast carcinoma with asymptomatic metastasis to the gallbladder. *Singapore Med J*. 2012; 53(7):e136-8.
 9. Salita A, Rosado M, Mack K, Pui J, Zekman R, Dinnan K. Metastatic lobular carcinoma of the breast found incidentally on pathology following cholecystectomy for chronic cholecystitis: A case report. *Int J Surg Case Rep*. 2021; 80:105612.
 10. Missori G, Serra F, Prestigiacomo G, Ricciardolo AA, Brugioni L, Gelmini R. Case Report: Metastatic breast cancer to the gallbladder. *F1000Res*. 2020; 9:343.
 11. Fleres F, Rossitto M, Foti A, Macrì A, Cucinotta E. Metastasis of the gallbladder from the breast cancer. *Ann Ital Chir*. 2014; 85(ePub): S2239253X14023470.
 12. Kolling S, Ventre F, Geuna E, Milan M, Pisacane A, Boccaccio C, Sapino A, Montemurro F. "Metastatic Cancer of Unknown Primary" or "Primary Metastatic Cancer"? *Front Oncol*. 2020; 9:1546
 13. Barbieri E, Anghelone CAP, Gentile D, La Raja C, Bottini A, Tinterri C. Metastases from Occult Breast Cancer: A Case Report of Carcinoma of Unknown Primary Syndrome. *Case Rep Oncol*. 2020; 13(3):1158-1163.