

# Breast carcinoma with asymptomatic metastasis to the gallbladder

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**ABSTRACT** The biliary tract is an unusual site of metastasis from breast carcinoma, and this has rarely been reported in the literature. We report the case of a 42-year-old woman diagnosed with invasive lobular carcinoma of the breast who underwent laparoscopic cholecystectomy for an incidental finding of gallbladder wall thickening on ultrasonography, which was subsequently confirmed to be consistent with metastasis from the breast primary.

**Keywords:** biliary metastasis, breast carcinoma, gallbladder metastasis, infiltrating lobular carcinoma  
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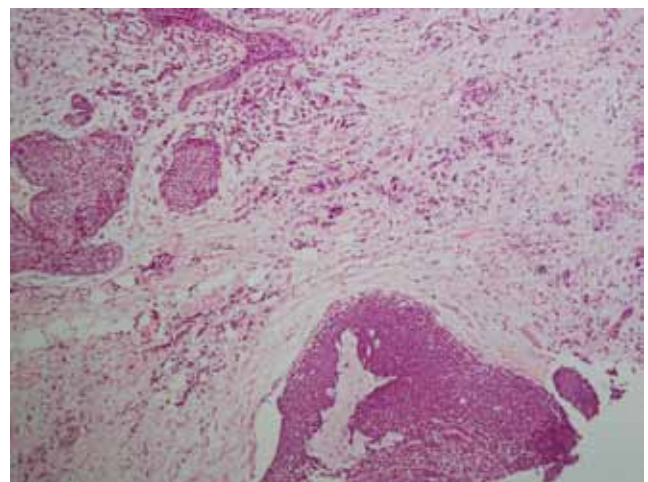
## INTRODUCTION

Metastatic breast cancer is diagnosed in less than 10% of patients at presentation, with bones, lungs and liver being the common sites of involvement. Less common metastatic sites are the adrenals, ovaries, pericardium, thyroid and bone marrow.<sup>(1)</sup> Metastasis to the gastrointestinal tract and eye has infrequently been reported.<sup>(2,3)</sup> The gallbladder as the site of metastasis from breast carcinoma is extremely rare, and only a few such case reports have been published to date. Here, we report a case of infiltrating lobular carcinoma with asymptomatic metastasis to the gallbladder.

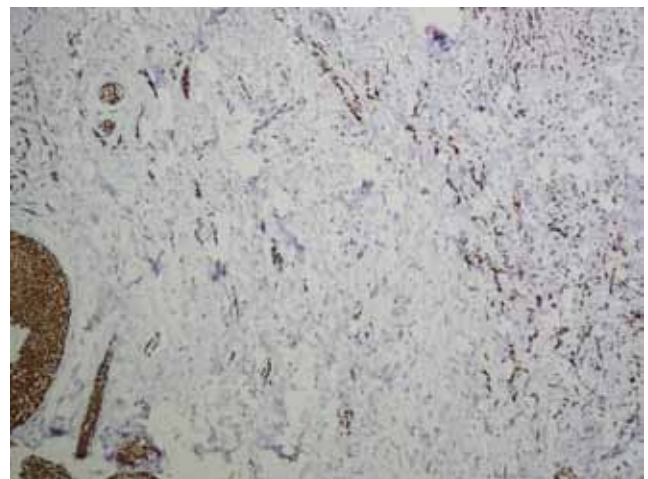
## CASE REPORT

A 42-year-old premenopausal woman presented with a lump in her left breast for nine months, which had gradually increased in size. She did not have any risk factors for breast cancer. On review, she reported pain in the lower back for three months without any neurological symptoms. Breast examination revealed an ill-defined palpable area in the left breast in the lower outer quadrant close to the limbus, with overlying skin tethering. The contralateral breast was normal, with impalpable axillary nodes. Mammograms did not show any dominant lesion or pleomorphic microcalcifications. However, ultrasonography (US) of the left breast revealed ductal thickening in the retro-areolar area, with a small nodule with posterior enhancement measuring 6.4 mm × 3.5 mm. This was followed by a US-guided Tru-cut biopsy of the left breast lesion, which revealed infiltrating lobular carcinoma (Fig. 1). The tumour was positive for oestrogen (Fig. 2) and progesterone receptors.

The liver was normal on US, but there was a focal area of thickening in the body of the gallbladder that was encroaching into the lumen without any stones or sludge, with a normal common bile duct (Fig. 3). Subsequent computed tomography of the liver showed a contracted gallbladder without any evidence



**Fig. 1** Photomicrograph shows lobular carcinoma of the breast *in situ* and invasive (Haematoxylin & eosin, × 100).



**Fig. 2** Photomicrograph shows lobular carcinoma of the breast that is positive for oestrogen receptors (Immunohistochemical staining, × 100).

of a lesion. The patient's bone scintiscan was suspicious for a possible area of increased uptake in the left sacroiliac joint, which on magnetic resonance imaging revealed abnormal intensity

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**Fig. 3** US image shows a focal area of thickening in the body of the gallbladder.

signals in the sacrum, ileum, ischium and the lower lumbar spine, suggestive of metastasis.

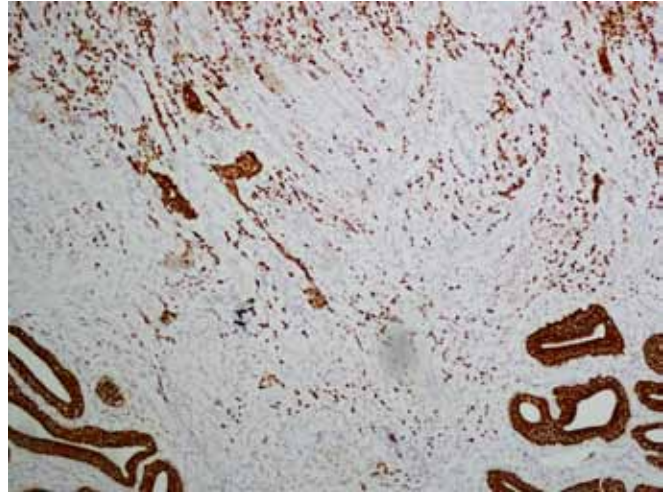
In view of the US findings of the gallbladder, a diagnostic laparoscopy with or without laparoscopic cholecystectomy was advised so as to differentiate possible metastatic disease in the gallbladder from a primary gallbladder neoplastic lesion. Diagnostic laparoscopy revealed a gallbladder that appeared to be thick-walled. There were no peritoneal deposits or ascites, and the liver and pelvic organs were grossly normal. A cholecystectomy was performed, and the postoperative course was uneventful. Histopathology of the gallbladder revealed involvement by an infiltrating malignant neoplasm composed of cords and nests of malignant neoplastic cells showing moderate amount of eosinophilic cytoplasm containing irregular hyperchromatic nuclei. In areas of the neoplastic cells, an 'Indian-file' pattern was appreciated, and the neoplastic cells were positive for cytoplasmic mucin and cytokeratin-7 (Fig. 4) and negative for cytokeratin 20 and E-cadherin. The tumour was positive for oestrogen (Fig.5) and progesterone receptors.

The patient was subsequently started on tamoxifen. However, in view of the local progression of the disease, she was started on systemic chemotherapy, to which she responded well. This was followed by simple mastectomy and radiotherapy to the chest wall and axilla. Until her last follow-up, the patient was asymptomatic with stable disease.

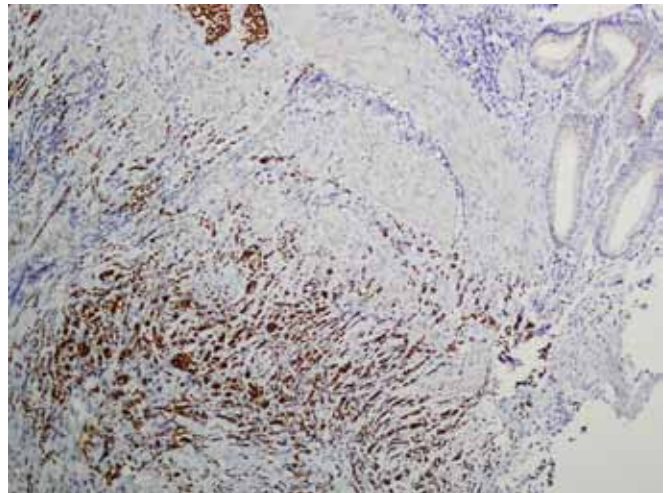
## DISCUSSION

Most patients are diagnosed with metastatic breast cancer after having been treated for stage I, II or III disease. On the contrary, less than 10% of patients with breast cancer have evidence of metastasis at presentation.<sup>(4)</sup> Contiguous, lymphatic and haematogenous routes are documented and well-understood mechanisms of metastasis from breast cancer. There are several reports in the literature regarding unusual metastatic sites with involvement of the gastrointestinal and biliary systems. According to an autopsy study involving 337 cases, 16.4% of patients with primary breast cancer had gastrointestinal metastasis.<sup>(5)</sup>

Gallbladder is a rare site of metastasis from malignant diseases. In one large autopsy study of patients with known



**Fig. 4** Photomicrograph shows tumour cells in the gallbladder that are positive for cytokeratin 7 (Immunohistochemical staining,  $\times 100$ ).



**Fig. 5** Photomicrograph shows tumour cells in the gallbladder that are positive for oestrogen receptors (Haematoxylin & eosin,  $\times 100$ ).

malignancy, metastatic involvement of the gallbladder was found in only 5.8% of patients,<sup>(6)</sup> and breast cancer leading to metastasis to the gallbladder has been reported to occur in 4%–7% of patients.<sup>(7)</sup> The reported time interval between the treatment of the primary breast carcinoma and the detection of gallbladder metastasis may vary from 18 months to more than ten years.<sup>(8)</sup> In addition to breast, haematogenous metastasis to the gallbladder has also been reported in association with melanoma, renal, cervical, gastric and lung carcinomas.<sup>(9-11)</sup>

Findings from autopsy series of gallbladder metastasis have shown that secondary haematogenous metastasis to the gallbladder progresses from small flat nodules below the mucosal layer to pedunculated lesions, seldom exceeding a few millimetres in size. This may partly explain why most gallbladder metastases have an asymptomatic presentation and why they are usually reported in autopsy studies. The most common symptomatic presentation is acute cholecystitis; however, obstructive jaundice, perforation leading to biliary peritonitis and haemobilia have also been described.<sup>(7,12,13)</sup>

Invasive lobular carcinoma accounts for 8%–14% of all breast cancers, and has distinctive clinical and biological

characteristics as compared to infiltrating ductal carcinoma. There is evidence in the literature to support the differences in the metastatic patterns of infiltrating lobular and infiltrating ductal carcinoma of the breast.<sup>(17)</sup> In one large autopsy study, invasive lobular carcinoma exhibited more involvement of peritoneum/retroperitoneum, leptomeninges, hollow viscera and myocardium.<sup>(18)</sup> It has been demonstrated that the loss of expression of the cell-cell adhesion molecule, E-cadherin in lobular carcinoma may decrease the adhesiveness of the cells and facilitate this pattern of metastasis.<sup>(19)</sup>

In conclusion, metastasis to the gallbladder is associated with a poor prognosis, as the disease is usually widespread at the time of diagnosis. We emphasise the need for a thorough evaluation of any gastrointestinal symptoms pertaining to the biliary tree, or any findings of incidental gallbladder lesions detected on imaging, in order to have a complete assessment of the stage of disease.

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