

# Metastatic breast cancer mimicking cholecystitis

## *A rare clinical presentation*

*Haitham Al-Rawi, MSc, PhD, Mohammad Al-Jafari, MSc, FRCPath, Hitesh Mathew, MBBS, MSc.*

### ABSTRACT

لقد سجلنا حالة لامرأة عمرها 61 عاماً كانت تعاني من ألم في الصدر والشرسوف وكان الإنطباع السريري أنها تعاني من التهاب الحويصلة الصفراوية والتي تم استئصالها فيما بعد. أظهر الفحص النسيجي الإصابة بالالتهاب المزمن وانتقالات سرطانية مصدرها الثدي. بعد ذلك تمت الفحوص الإشعاعية والسريرية والتي أظهرت تليف موضعي في الثدي الأيسر. وقد أكد فحص الخزعة النسيجية الإصابة بسرطان الثدي. وبعد ذلك تمت المعالجة الجراحية والكيميائية للورم. لاحقاً وبعد 5 سنوات من استئصال الحويصلة الصفراوية توفيت المريضة نتيجة لانتشار الشامل لسرطان الثدي. تظهر هذه الحالة الأهمية الكبرى للفحص النسيجي العياني والخلوي للحويصلة الصفراوية.

We report a case of a 61-year-old lady who presented with central chest and epigastric pain. A clinical diagnosis of cholecystitis was established, and a cholecystectomy was carried out. Microscopic examination of the gallbladder showed chronic cholecystitis and metastatic carcinoma of probable breast lobular carcinoma origin. The report was followed by further clinical and mammographic examination, which showed a focal area of thickening in the left breast. Core biopsy of this lesion confirmed the diagnosis of lobular carcinoma of the breast. Her tumor was treated with surgery followed by chemo/hormone therapy. The patient died 5 years after the cholecystectomy from disseminated breast malignancy.

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*From the Department of Histopathology, Warrington and Halton Hospitals, NHS Trust, Warrington, Cheshire, United Kingdom.*

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*Address correspondence and reprint request to: Dr. Hitesh Mathew, Histopathology Department, Warrington Hospital, Lovely Lane, Warrington, Cheshire, WA5 1QG, United Kingdom. Tel. +44 (78) 34358081. Fax. +44 (19) 25662043. E-mail: drhigem@yahoo.com*

Breast cancer is known to metastasize to all organs, and its manifestations are protean. It is almost impossible to predict, which organ will be invaded by the disease.<sup>1</sup> Approximately 10-15% of patients with breast cancer have an aggressive disease, and develop distant metastases within 3 years after the initial detection of the primary tumor.<sup>2</sup> There are few reports of metastatic breast cancer in the gall bladder; some autopsy studies state the incidence as 5.8%.<sup>3</sup> The possibility of malignancy should always be considered in the elderly as signs and symptoms are vague and can often be difficult to identify. This case is presented to highlight the importance of careful macro- and microscopic examination of routine gallbladder specimens, as the features of metastatic disease can be subtle.

**Case Report.** A 61-year-old woman presented with a history of intermittent central chest and epigastric pain in May 2005. Her pain was described as a "heavy pressure". Physical examination did not reveal any abnormalities. She was admitted for further tests. On admission, the patient was hemodynamically stable. The laboratory results were as follows: Troponin I - <16 ug/L (normal value; <16); hemoglobin - 11.9 g/dl (normal value; 11.5-16.5); total bilirubin - 15 umol/L (normal value; 0-17); aspartate transaminase - 37 IU/L (normal value; 0-17); alanine transaminase - 42 IU/L (normal value; 0-40); gamma glutamyl transpeptidase - 78 IU/L (normal value; 0-55). Bone profile showed an alkaline phosphatase of 168 IU/L (normal value; 39-118). Cholesterol was 6.3 mmol/L (normal value; 3.1- 5.2). Her renal profiles, total protein, albumin, globulin, and C-reactive protein were normal. An

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ultrasound scan of her abdomen showed gall stones. A clinical diagnosis of cholecystitis was established, and an elective laparoscopic cholecystectomy was carried out 3 months later.

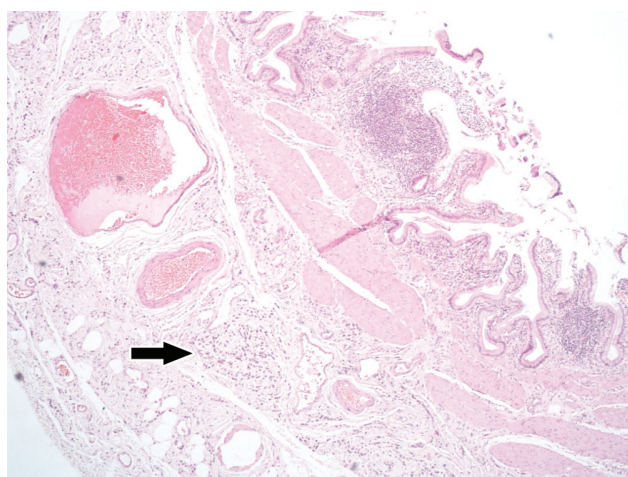
The resected gallbladder measured 70x30x15 mm. The lumen contained multiple yellow-white stones varying in sizes from 5-10 mm. The mucosa was velvety, and the wall was up to 3 mm thick. No focal lesions were identified. Microscopically, sections of the gallbladder showed moderate chronic cholecystitis, associated with reactive lymphoid follicles and pyloric metaplasia. The serosa and adjacent fat showed focal infiltrates of cells with rounded nuclei, and small cytoplasmic vacuoles (Figures 1 & 2). The cells were seen individually and arranged in single files. Immunohistochemistry showed positive reaction for these cells with pan cytokeratins, epithelial membrane antigen, cytokeratin (CK) 7, and estrogen receptor. The cells were negative for leukocyte common antigen, CK20, thyroid transcription factor-1, and vimentin. A histopathological diagnosis of chronic cholecystitis and metastatic carcinoma of probable breast lobular carcinoma origin was established.

Following the above report, the patient was re-examined and found to have a focal area of thickening (40x50 mm) in the upper outer quadrant of the left breast. She also revealed that she had previous breast lumps removed 30 years before, and that she had a breast cyst drained 10 years earlier. A mammogram was arranged, and it showed a new asymmetrical density in the upper half of the left breast, which was not present in previous films from 2002. Ultrasound scanning also showed vague attenuation in this area, and a core biopsy was recommended.

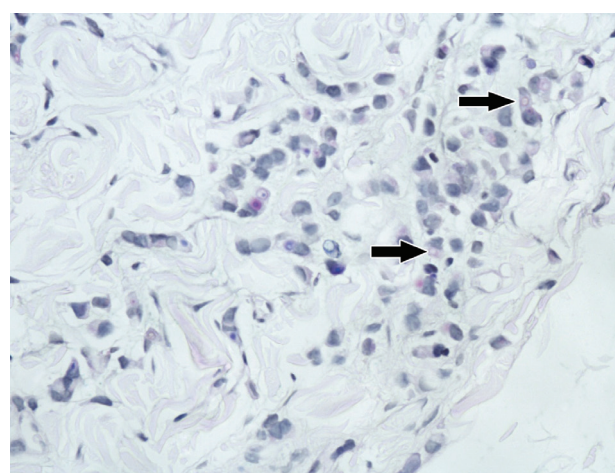
The core biopsy of the lesion showed a grade 2 infiltrating lobular carcinoma (tubule 3, pleomorphism 3, and mitosis 1). Her alkaline phosphatase remained elevated (182 IU/L) and cancer antigen 19,9, and cancer antigen 125 were also elevated. Carcino embryonic antigen was 5.09 (normal value; <4 ug/L) and alpha-feto protein was normal. Multiple bony lytic lesions involving the vertebral column, ribs, sternum, and iliac bones were seen on the bone scan. She underwent the following chemo/hormone therapy due to the advanced nature of her disease; initial treatment was with Anastrozole, and a definite response was achieved.

Disease progression occurred in November 2007. Anastrozole was switched to Tamoxifen in August 2008. Her symptoms did not improve with Tamoxifen, and she presented with increasing pain, ascites, and bilateral pleural effusion. Her treatment was switched to Fulvestrant; however, the disease progressed further in January 2009. She was then treated with palliative chemotherapy, achieving a definite response. This treatment was completed in May 2009. Further disease progression in August 2009 was treated with second line chemotherapy (Docetaxel), achieving only partial response. Treatment was completed in December 2009. In March 2010, she was transferred to her local hospice where she died in May 2010, 5 years after the initial diagnosis.

**Discussion.** Breast cancer spreads through lymphatic, hematogenous, or transcoelomic routes. It usually spreads to the lungs, liver, and bone. Less



**Figure 1** - Low power view of gall bladder wall showing a focus of lobular carcinoma cells.



**Figure 2** - High power view of lobular carcinoma cells showing intra cytoplasmic mucin.

frequent sites include central nervous system, uterine cervix, endocrine organs, peritoneal cavity, and gall bladder. Malignancies most likely to metastasize to the gallbladder are malignant melanoma, breast, gastric, pancreatic, colonic, cervical, and renal cell carcinomas. Case reports of metastasis in gall bladder have also shown frequent involvement of cystic duct lymph node. While 60% of women who develop distant breast cancer metastases will do so within 24 months of treatment of the primary cancer, metastases may become evident as late as 10-20 years after this initial treatment.<sup>3</sup> Studies have also shown no statistically significant difference in the frequency of metastases to common metastatic sites (such as the liver, bone, and pleura), and type of primary breast cancer with the exception of the lungs, in which infiltrating ductal carcinoma metastases are more frequent. By contrast, a statistically highly significant prevalence of invasive lobular carcinoma metastases to the peritoneum/retroperitoneum, hollow viscera, internal genital organs, leptomeninges, and myocardium is seen.<sup>4</sup>

A case of breast cancer also presenting as cholecystitis has been previously described in the literature.<sup>5</sup> The cases emphasize the significance of careful examination of routine gall bladder specimens, as the features of metastatic disease can be subtle, and be overlooked at low power as inflammation. Further evaluation with special

stains (alcian blue PAS), and immunohistochemistry may be required. This is especially true in the light of case reports of undifferentiated carcinoma of the gallbladder, mimicking lobular carcinoma of the breast. The literature supports aggressive surgical treatment, combined with systemic therapy in cases of breast cancer with extrahepatic biliary metastasis as it can offer significant palliation and better survival.

In conclusion, although the presentation described in this report is rare, both breast cancer and cholecystitis are relatively common. In elderly patients presenting with unexplained symptoms, metastatic cancers should always form part of the differential diagnosis.

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