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Breast carcinoma metastatic to the gallbladder and urinary bladder

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Abstract. – We present a patient with a history of infiltrating lobular breast carcinoma that metastasized to both the biliary and urinary tract after a ten year disease-free period following mastectomy and chemoradiotherapy. The patient presented with acute cholecystitis; imaging and histopathology revealed infiltrating lobular carcinoma of the gallbladder and urinary bladder. This report emphasizes the importance of long-term follow up in patients with a history of breast cancer and maintaining a high degree of suspicion for diagnosis of metastatic disease.

Key Words:

Metastatic, Breast, Carcinoma; Gallbladder, Urinary, Bladder, Cholecystitis.

Introduction

Breast carcinoma is the second leading cause of female cancer deaths and the most common malignancy among women, affecting nearly 1 in 8 females[1]. Frequent sites of metastases include lymph nodes, lungs, bone, liver, adrenals, and meninges[2]. Breast carcinoma metastasizing to either the gallbladder or urinary bladder is rare with few cases reported in the English literature[3-9]. We report a patient with simultaneous metastatic spread of infiltrating lobular carcinoma of the breast to the gallbladder and urinary bladder following a ten year post-treatment asymptomatic period who presented with acute cholecystitis.

Case Report

A 46-year-old female underwent a modified radical mastectomy with axillary dissection for carcinoma of the left breast. Histopathology confirmed invasive lobular carcinoma, classic type. Specimen margins were noted to be tumor free with 12 of 14 nodes positive, consistent with stage III disease[10]. Estrogen and progesterone immunohistochemical stainings were moderately positive; adjuvant radiation and chemotherapy was instituted. The patient was asymptomatic without recurrence for the following ten years on routine follow-up. However, she subsequently presented to the Emergency Department with right upper quadrant abdominal pain and episodes of nausea and emesis. A computed tomography (CT) scan of the abdomen and pelvis revealed a pelvic mass obstructing the right ureter causing right hydronephrosis and hydroureter. Thickening of the right lateral and posterior wall of the bladder was seen, as well as a large gallstone with pericholecystic fluid suggestive of acute cholecystitis. The patient was admitted and treated with intravenous antibiotics and her abdominal pain resolved. Flexible cystoscopy was performed demonstrating an erythematous, ulcerated lesion on the right lateral and posterior bladder wall. The bladder mass was biopsied and ureteral stenting was attempted but unsuccessful because of inability to pass a wire into the ureteral orifice. A percutaneous nephrostomy tube was placed in the right kidney to treat the hydronephrosis. Histopathology of the bladder lesion identified metastatic infiltrating lobular carcinoma, Her2/Neu+, ER/PR+ (Figure 1). The patient was started on chemotherapy with anastazole. Because of persistent symptomatic cholelithiasis, she underwent laparoscopic cholecystectomy, which was converted to an open cholecystectomy due to severe adhesions. Histopathology showed a large gallstone with metastatic infiltrating lobular carcinoma to the gallbladder with chronic cholecystitis (Figure 2).

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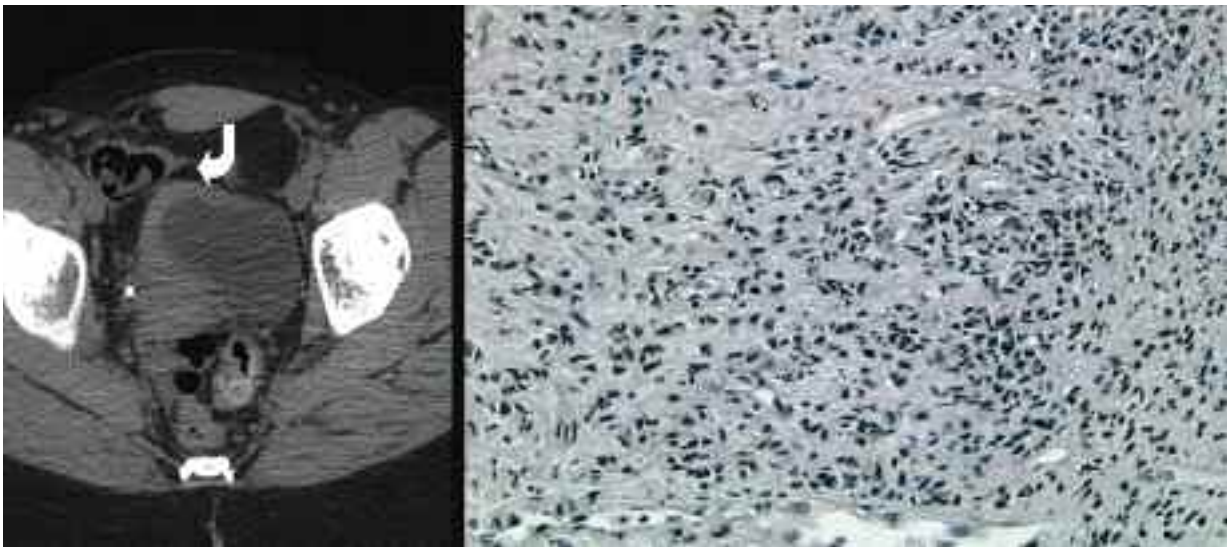

Figure 1. A patient with a distant history of breast cancer presents with metastases to the gallbladder and urinary bladder. (*Left*) CT urogram demonstrates a thickened bladder wall (curved arrow). (*Right*) Histopathology of the bladder lesion showed metastatic mammillary infiltrating lobular carcinoma (hematoxylin and eosin staining, low magnification). Pan cytokeratin, estrogen receptor, and progesterone receptor immunohistochemistry aided in confirming the diagnosis.

Discussion

This manuscript is the first to report breast cancer recurrence with metastases to both the gallbladder and urinary bladder presenting with abdominal symptoms. Breast cancer can spread by local lymphatic invasion as well as hematogenous dissemination. The most common organ systems associated with breast cancer metastases are bone, lung, liver, central nervous system, endocrine, and pericardium[2]. Primary tumors can metastasize to the gallbladder either by direct invasion of the porta hepatis or by hematogenous spread. Hematogenous spread to the gallbladder is more commonly seen with melanoma, renal cell, cervical, gastric, and lung[11-15]. Patients with metastatic disease to the gallbladder typically present with symptoms consistent with acute or

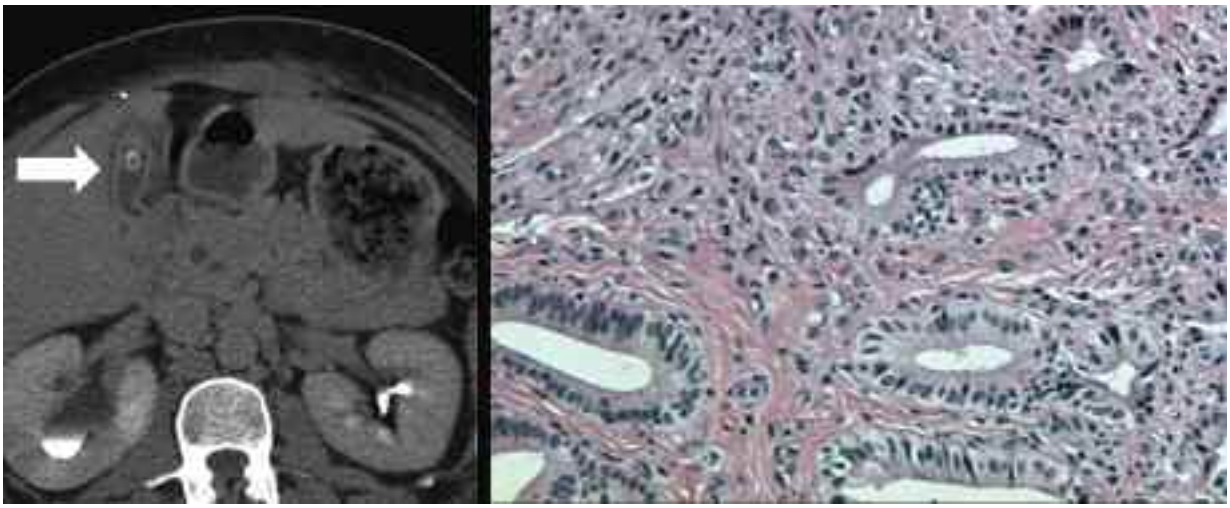

Figure 2. The patient presents with abdominal pain. (*Left*) CT scan of the abdomen demonstrates a thickened gallbladder wall, pericholecystic fluid, and a large gallstone (straight arrow). (*Right*) Histopathology of the gallbladder specimen following laparoscopic cholecystectomy showed metastatic invasive lobular carcinoma (hematoxylin and eosin staining, high magnification). The 6-cm tumor was present in the fundus body. Evidence of chronic cholecystitis also was seen.

chronic cholecystitis and obstructive jaundice[6,8]. Beaver et al.[5] reported a case of a 73 year old female with breast carcinoma who developed cholecystitis and underwent cholecystectomy. The pathological examination was showed metastatic breast carcinoma within the gallbladder specimen. Crawford et al.[9] reported two cases of metastatic breast cancer presenting as cholecystitis. Both patients had undergone a mastectomy several years prior to their biliary complaints[6]. Lobular carcinoma of the breast more frequently metastasizes to gynecologic organs, peritoneum-retroperitoneum, gastrointestinal, and the biliary system[16-19]. A large series noted that 3.1% of lobular carcinoma metastasized to the peritoneum-retroperitoneum compared with 0.6% of ductal carcinoma[17]. In our report, the original malignancy, metastatic bladder lesion, and gallbladder specimens were invasive lobular carcinoma.

Metastatic neoplasms of the bladder make up 2-14% of all malignant bladder tumors[20]. Common presenting symptoms include hematuria, incontinence, urgency, and flank pain from hydronephrosis. Tumors spread to the bladder most commonly by direct regional invasion from local organs, such as the colon, prostate, rectum, and cervix, or as metastases from distant sites, such as stomach, skin (melanoma), lung, and breast[21]. Breast carcinoma metastatic to the bladder is rare and accounts for roughly 3% of secondary bladder neoplasms[22]. The first reported cases of breast cancer metastatic to the bladder were from post-mortem reports[11]. In 1956, Ganem and Batal[21] performed a retrospective review of the literature and identified 16 cases of breast cancer metastatic to the bladder. In 1965, Perez et al.[23] reported 13 cases, 11 of which were discovered at autopsy. Abrams et al.[10] reported 4 cases with bladder metastasis from 1000 autopsies of patients with breast cancer. Goldstein[24] identified 4 cases of metastatic carcinoma to the bladder after reviewing 341 autopsy cases of patients who died of advanced carcinoma of the breast. Feldman et al.[22] noted that infiltrating lobular carcinoma, which accounts for less than 8% of all breast cancer cases, was responsible for 33% of the reviewed metastatic breast carcinoma to bladder cases. Pontes and Oldford[25] postulated that breast cancer metastasizes to the bladder via retroperitoneal involvement. Bladder metastases have been reported as late as 360 months after the initial diagnosis of breast cancer, with a mean of 90 months[26]. This is consistent with our patient who developed metastatic symptoms from her primary disease 96 months after initial diagnosis.

In conclusion, we present a patient with bladder and gallbladder metastases following a ten-year disease-free interval after treatment for T3N1M0 lobular breast carcinoma. Although the bones, lungs, and liver are the most common sites of spread of distant disease, metastases from breast cancer can be seen in many organs. Metastatic disease always should be included in the differential diagnosis of a patient with a history of invasive breast cancer and new onset abdominal pain. Symptoms of abdominal pain, flank pain, acute or chronic cholecystitis, hematuria, obstructive jaundice, and urinary incontinence can be the initial presenting signs of metastatic disease.

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