Case Report

Liver Metastasis in a Young Female Secondary to Breast Cancer: A Case Report

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Abstract

Breast cancer is common among females worldwide and is most commonly reported in women aged 30–40 years and less commonly in those aged <30 years. Presentation with liver metastasis is rare in breast cancer at all ages. Lactic acidosis in association with metastatic breast cancer is also rare. Here, the authors report a case of a 26-year-old female who presented with cholestatic jaundice, coagulopathy and ascites. Radiological examination showed evidence of infiltrating liver lesion. Computed tomography-guided liver biopsy confirmed the diagnosis of adenocarcinoma of breast origin based on the strong estrogen receptor positivity. Chemotherapy could not be initiated because of the patient's critical condition. Unfortunately, the condition deteriorated rapidly, and the patient died secondary to liver failure manifested with disseminated intravascular coagulation and lactic acidosis. This is a rare case of breast cancer in terms of age group (<30 years), site of metastasis at presentation and complication of metastatic breast cancer (type B lactic acidosis), and thus highlights the distinct features of such breast cancers.

Keywords: Breast cancer, lactic acidosis, liver metastasis, young female

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Received: 28-03-2017 **Revised:** 18-05-2017 **Accepted:** 10-07-2018 **Published:** 28-08-2019

INTRODUCTION

Breast cancer is the most common cancer among females worldwide,[1] including Saudi Arabia.[2] The majority of cases are diagnosed in women aged 30–44 years, and it is less commonly reported in those aged <30 years.[3] In addition, liver metastasis at presentation of breast cancer is found in <10% of patients.[4] Liver metastasis has been found to be an unfavorable independent prognostic factor, with the median survival being only 12 months.[5] In this report, the authors describe a case of a young female who presented with symptoms of cholestatic jaundice secondary to multifocal infiltrative liver lesions, which was later found to be metastatic breast adenocarcinoma. The aim of this case report is to add to the growing literature about breast cancer in women aged <30 years.

CASE REPORT

A 26-year-old female was admitted to the emergency room of our hospital with a 3-month history of intermittent, progressive, moderate-to-severe, dull-aching, epigastric and right hypochondrial abdominal pain. The pain was associated with nausea, anorexia and subjective weight loss with no known aggravating or relieving factors. In addition,

Access this article online	
Quick Response Code:	Website: www.sjmms.net
	DOI: 10.4103/sjmms.sjmms_49_17

How to cite this article: Al Qahtani SY, Al Argan RJ. Liver metastasis in a young female secondary to breast cancer: A case report. Saudi J Med Med Sci 2019;7:190-4.

there was no history of fever, night sweats, abnormal bowel habits and discoloration of urine or stool. The patient was not on any medications as well as did not have a history of smoking, alcohol or illicit drug abuse, or a family history of breast cancer.

On physical examination, the patient was conscious, alert and oriented to time, place and person. However, she was in abdominal pain and appeared cachectic, jaundiced and pale without any respiratory distress. Her vital signs were as follows: body temperature, 36.4°C; pulse rate, 108 beats/min; respiratory rate, 20 breaths/min; blood pressure, 100/60 mmHg; and oxygen saturation, 100% on room air. Systemic examination was positive for scleral jaundice, tender hepatomegaly with liver span of 17 cm, ascites in the form of positive shifting dullness and Grade 1 bilateral lower-limb pitting edema with no splenomegaly or other stigmata of chronic liver disease.

Initial investigations showed microcytic hypochromic anemia with a hemoglobin level of 10 g/dL. Other laboratory investigations were as follows: mean corpuscular volume, 79.7 fL; mean corpuscular hemoglobin, 25.9 pg; direct hyperbilirubinemia with mainly cholestatic pattern of liver enzyme elevation; total bilirubin, 5.1 mg/dL; direct bilirubin, 4.6 mg/dL; total protein, 8.2 mg/dL; albumin, 2.2 mg/dL; alanine transferase, 115 U/L; aspartate transferase, 645 U/L; lactate dehydrogenase, 768 U/L; alkaline phosphatase, 828 U/L; and gamma-glutamyl transpeptidase, 1184 U/L. Results of coagulation tests were as follows: prothrombin time, 16 s; international normalized ratio, 1.34; and partial thromboplastin time, 39.3 s. In addition, erythrocyte sedimentation rate was 86 mm/h and the level of C-reactive protein was 3.3 mg/dL.

Abdominal ultrasound was remarkable for cirrhotic liver with a hyperechoic, irregularly shaped lesion infiltrating the lateral segment of the right lobe of the liver. There was evidence of central intrahepatic biliary dilatation and diminished portal vein flow as well as moderate-to-severe ascites. Ascitic fluid examination showed a normal cell count and a normal level of protein and lactate dehydrogenase. Results of Gram stain and culture were nonremarkable. Cytology could not be done because of inadequate cellularity. Serum ascitic albumin gradient was 1.6 g/dL.

Based on the findings, the patient was admitted as a case of cholestatic jaundice, and investigations were done to rule out any underlying infectious autoimmune or malignant diseases. Tests for hepatitis A, B, C, Epstein–Barr virus, cytomegalovirus, schistosomiasis and autoimmune profiles (antinuclear antibody, antimitochondrial antibody, anti-smooth muscle antibody and anti-liver–kidney microsomal antibody) were negative. Tumor marker tests were negative for alpha-fetoprotein and carbohydrate antigen (CA) 19-9. However, the level of CA 125 was 219.3 U/ml and that of CA 15-3 was 276.2 U/ml.

Computed tomography (CT) of the abdomen revealed an enlarged liver with multifocal infiltrative hypodense lesions and massive ascites [Figure 1]. Magnetic resonance imaging of the liver showed hepatomegaly and diffuse fat edema with an area of severe fat deposition. In addition, a hemorrhagic necrosis corresponding to a geographical area of mixed density was noted on the CT scan. Esophagogastroduodenoscopy showed four cords of Grade 2 esophageal varices with cherry red spots.

The patient was started on propranolol (20 mg once daily) along with furosemide (40 mg once daily) and spironolactone (100 mg once daily). A CT-guided liver biopsy was carried out after draining ascites using a pigtail catheter. On Day 12 postadmission, the patient's fever rose to 38.5°C. Ascitic fluid analysis showed a white blood cell (WBC) count of 23,750 cells/mm^3 (neutrophils, 83%; lymphocytes, 7% and monocytes, 10%), which was consistent with the diagnosis of spontaneous bacterial peritonitis. The patient was started on piperacillin–tazobactam (4.5 g intravenous every 8 h). On the 2nd day of initiating this treatment, the fever resolved as well as a repeated fluid analysis showed a WBC count of 47 cells/mm^3 (neutrophils 7% and lymphocytes 66%).

Results of the arterial blood gas analysis were as follows: pH, 7.36; partial pressure of carbon dioxide, 22.3 mmHg; and bicarbonate level, 14.9 mEq/L. Anion gap was 26 mEq/L, and lactic acid levels were 16.9 mmol/L. Because of the very high WBC count in the ascitic fluid and development of high anion gap metabolic acidosis due to lactic acidosis, a CT scan of the chest and abdomen was done to rule out perforation, localized collection or abscesses, and the results were unremarkable. However, due to disseminated intravascular coagulation (DIC), the patient's coagulopathy worsened. Coagulation tests revealed a prothrombin time of 17 s and an international normalized ratio of 1.34. In addition, partial thromboplastin time was 44.8 s, fibrinogen level was 104 mg/dL and fibrin degradation product levels were >10 to <40 μg/ml, all of which were attributed to liver failure.

Liver biopsy showed metastatic adenocarcinoma likely secondary to breast origin, as it was strongly positive for estrogen receptors [Figure 2]. The patient informed that she

had noted a mass in the left breast about 4–5 years ago but had not taken any action. Physical examination revealed a hard mass in the left breast that was fixed to the overlying skin with nipple retraction. This was confirmed on chest CT scan [Figure 3]. As the patient was in a critical condition, chemotherapy could not be initiated. The patient died on Day 28 postadmission secondary to liver failure manifested with lactic acidosis and DIC.

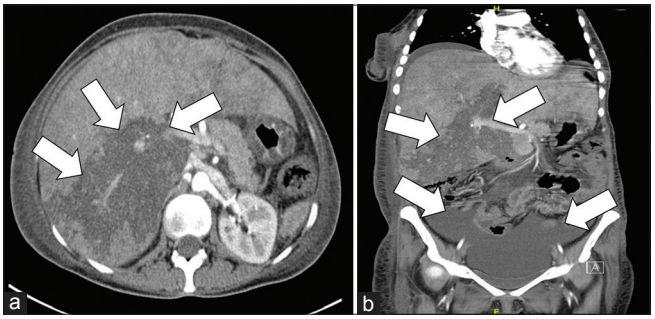

Figure 1: (a) Computed tomography scan of the abdomen (coronal view) showing enlarged liver with multifocal infiltrative hypodense lesions associated with internal hyperdensities, likely representing hemorrhage; (b) computed tomography scan of the abdomen (sagittal view) demonstrating the same findings as above in addition to massive ascites

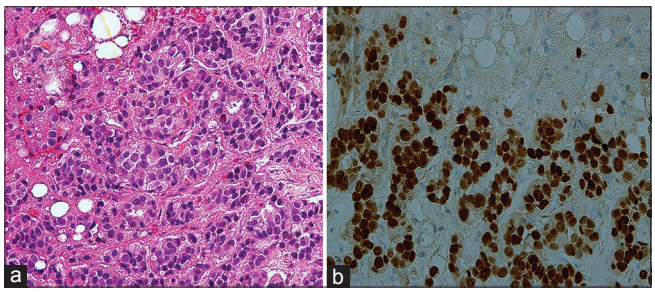

Figure 2: (a) Liver biopsy, intermediate power, showing abnormal cell-forming glands and large nuclei. Hyperchromatic nucleoli with increased mitosis. (b) Liver biopsy showing diffuse, strong staining of estrogen receptor

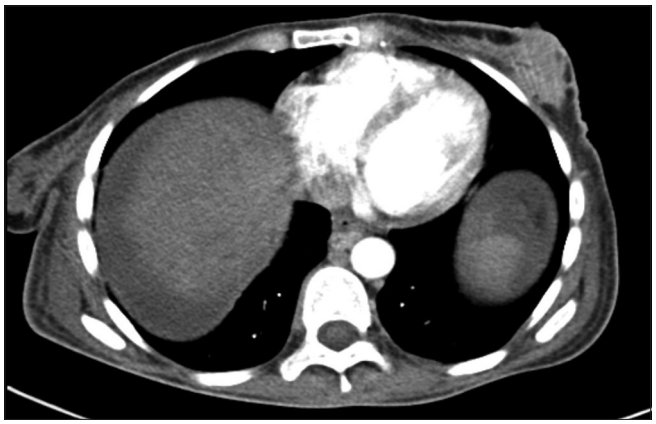

Figure 3: Computed tomography scan of the chest: Selective enhanced image demonstrating a relative well-defined hyperdense left retroareolar breast lesion with speculated borders associated with ipsilateral skin thickening, inseparable from pectoralis muscle posteriorly (no microcalcification or cell invasion seen,); contralateral breast shows heterogeneous parenchyma

DISCUSSION

Breast cancer is a leading cause of cancer deaths among women of various ethnic groups.[1] The crude incidence rate and age-standardized incidence rate in female breast cancer are increasing annually. In Saudi Arabia, Alghamdi *et al.*[3] reported 1152, 1308 and 1473 female breast cancer cases for the years 2008, 2009 and 2010, respectively. Further, the majority of breast cancer cases are diagnosed in women aged 30–44 years (38.6%) and 45–59 years (31.2%). Further, it is least commonly diagnosed in women aged 15–29 years (10%) and >75 years (10.2%).[3]

Similarly, in Oman, the median age of breast cancer diagnosis is 48 years, while females aged <20 years and 20–29 years account for only 0.1% and 6.2% of the diagnosis, respectively.[6] In a long-term study of the Asian population (1970–2002), the prevalence of breast cancer among women aged <30 years was found to be 12%.[7] Collectively, the findings of the studies and recommendations indicate that breast cancer is uncommon in younger aged females.

According to the American Cancer Society's recommendations for breast cancer screening, women aged 40–44 years should be provided an opportunity to begin annual screening, and it should be initiated in all women aged >45 years.[8] However, owing to its lower frequency, there is no recommendation to screen females aged <30 years. In the current case as well, initially, breast cancer was not considered as a possible cause of the presentation because of the patient's age. A history of breast mass and findings on chest CT were only found retrospectively after the diagnosis was made by histopathology of the liver biopsy. Therefore, the authors recommend that in women with unexplained liver lesion, a history and physical examination for breast mass should be carried out.

Although age is the strongest risk factor, it may vary within age groups as well. Studies have shown that women with genetic mutations in *BRCA1* and *BRCA2* genes, family history of breast cancer and radiation therapy to the chest including breasts, especially before the age of 30 years, have a higher chance of developing breast cancer at a younger age.[9] Our patient did not have a family history of breast cancer, and genetic studies could not be carried out.

It is less common for women to present with Stage IV breast cancer, as highlighted in a recent study in which,

of the 4543 breast cancer patients studied, only 3.2% had metastatic disease at presentation.[10] Similarly, a recent study found that in women aged ≤40 years, the rate of metastasis at presentation is as low as 2.5%.[11] With respect to the site of metastasis, breast cancer most commonly metastasizes to the bone followed by the lung, liver and brain.[4] In a study that analyzed Stage IV breast cancer trends in patients over three decades, it was found that the rate of liver metastasis ranged from 1.28% to 4.5%.[12] Although metastasis in general, and liver metastasis specifically, is less common at initial presentation, it was the case with our patient, indicating Stage IV breast cancer at presentation. The late diagnosis (4–5 years after the breast mass was initially observed by the patient) as well as aggressiveness of the disease in this age group may have resulted in the advanced clinical course observed.

The breast cancer survival rates vary by stage at diagnosis. In the United States, the 5-year survival rates in Stage I breast cancer patients across different ethnicities range from 94% to 98%, whereas for Stage IV patients, the survival rates range from 26% to 40%.[13] Surprisingly, younger age alone has been shown to be associated with poorer prognosis. In Saudi Arabia, according to Elkum *et al.*,[14] double-negative estrogen and progesterone receptor status and Grade III tumors are significantly higher in women aged ≤40 years than among those aged >40 years; both these factors are associated with poorer prognosis. In addition, they found that the 10-year disease-free survival was significantly lower in the younger group (60%) compared with the older group (70%).[14] Similarly, younger age of breast cancer has also been found to be an independent negative prognostic factor in a study from Japan.[15] Furthermore, Her2-positivity and hormonal receptor negativity have been shown to be associated with poor prognosis in breast cancer patients aged <25 years.[16] Both of these markers were associated with liver metastasis at the initial presentation in prior studies,[4,17] which could explain the aggressive course of disease in this age group.

Site of metastasis has been demonstrated to be an independent prognostic factor to predict breast cancer survival,[4,5] with the lowest median survival being in patients with brain metastasis (3 months) followed by multiple (9 months) and liver metastasis (12 months).[5] Specifically, liver metastasis in patients with *de novo* disease has been shown to be an independent prognostic factor for overall survival.[17]

Although our patient was estrogen receptor positive, which is associated with better outcome,[18] she presented with a rapidly deteriorating clinical course, which is likely due to markedly infiltrating liver metastasis. Additional factors for such a course could be young age and late presentation.

Metastasis followed by infection is the most common cause of death in patients with breast cancer. However, hepatic failure secondary to malignancy in general,[19] and specifically to breast cancer,[20] is not common. Our patient had extensively infiltrating liver lesion, which resulted in liver failure manifested with lactic acidosis and DIC. Type B lactic acidosis has been reported to be an oncologic emergency most commonly associated with hematological malignancies such as leukemia or lymphoma, but rarely associated with solid malignancies such as breast cancer. Recently, Nair and Shah,[21] in their review of literature, found that when solid tumors do present with lactic acidosis, it is mostly in cases with lung cancers (>50% cases) and liver metastasis occurred in almost all cases,[21] similar to the case reported here. They also found that, to date, only six cases of breast cancer presenting with Type B lactic acidosis had been reported, making the current report only the seventh such case to be reported in the literature. Similar to our patient, most such patients had a fatal outcome within hours or days of diagnosis. The best treatment is early initiation of aggressive chemotherapy;[21] unfortunately, owing to our patient's critical condition at the time of diagnosis, chemotherapy could not be initiated.

CONCLUSION

Breast cancer in young women and liver metastasis at presentation has a low frequency, poor prognosis and low survival rates. Lactic acidosis in association with metastatic breast cancer is rare and is especially seen in patients with extensive liver metastasis. Early diagnosis and prompt initiation of chemotherapy are essential to improve survival.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient's father has given his consent for his daughter's images and other clinical information to be reported in the Journal. The patient's father understands that his daughter's name and initials will not be published, and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

Peer review

This article was peer reviewed by one independent and anonymous reviewer.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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