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Simultaneous breast cancer and hepatocellular carcinoma in a male patient with alcoholic liver cirrhosis and a normal serum alpha-fetoprotein level

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ABSTRACT

Male breast cancer is rare, accounting for about 1% of all breast cancers. Hepatocellular carcinoma (HCC) is associated with liver cirrhosis in 70%–80% of cases; serum alpha-fetoprotein level is normal in less than half of HCC cases. We describe an 80-year-old male patient who experienced nausea and abdominal pain after food intake. On physical examination, a large, protruding, lobulated, and hard mass with skin discoloration was observed in the area of left breast. The serum alpha-fetoprotein level was normal. Ultrasonography (US) of the abdomen showed findings compatible with cholelithiasis, acute cholecystitis, liver cirrhosis, and a mixed-echoic tumor in segment 6 (S6) of the liver. Contrast-enhanced computed tomography (CT) with arterial and portal venous phases demonstrated the typical findings of cholelithiasis and acute cholecystitis; it also revealed a nodular liver surface, and a hypervascular liver tumor with an early washout pattern. Therefore, liver cirrhosis and HCC in S6 of the liver were suspected. A huge, irregular, lobulated mass with interior septation, solid and fluid components, and an enhanced solid component was also found in the subareolar region of the left breast. US-guided biopsy of the liver tumor was performed and a diagnosis of HCC was established.

Laparoscopic cholecystectomy and an excision of the left breast mass were performed. The breast mass was pathologically confirmed to be infiltrating ductal carcinoma not otherwise specified and with predominantly cystic degeneration. The patient received chemotherapy with tamoxifen for the breast cancer, and transarterial chemoembolization for the HCC. Concomitant breast cancer and HCC in a male patient were rarely reported in the literature. Herein, we have discussed the possible relationship of these two disease entities.

1. Introduction

Male breast cancer is rare, accounting for approximately 1% of all breast cancers, and has an incidence of only 0.7 per 100,000 male population.[1–4] A hormonal imbalance with elevated estrogen and decreased testosterone levels may play an important role in the development of male breast cancer.[5] Hepatocellular carcinoma (HCC) is a much more common cancer, and is associated with liver cirrhosis in 70%–80% of cases.[2] Liver cirrhosis is shown to be associated with an increased level of estrogen, and is therefore related to breast cancer.[6,7] An alteration in hormonal metabolism may contribute to the coexistence of HCC and breast cancer in male patients. Although a serum alpha-fetoprotein (AFP) level greater than 400 ng/mL has been shown to have high specificity (100%) for the diagnosis of HCC, it has low sensitivity (about 20%) and is present in <50% patients.[8,9] However, the AFP levels are normal in up to 30% of HCC cases,[9,10] and may be elevated in a number of metastatic liver diseases.[11]

2. Case report

An 80-year-old male patient suffered from nausea and

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abdominal pain after food intake. On physical examination, a large, protruding, lobulated, and hard mass with skin discoloration was observed at the left chest wall, in the area of the left breast (Fig. 1). A history of alcoholism for many years was noted. The body mass index (BMI) was 18.7 kg/m^2 and therefore within the normal limit (body height, 150 cm; body weight, 42 kg). The blood analysis revealed a mildly elevated white blood cell count (11,800/μL; normal value, 4,500–11,000/μL), increased fasting glucose (116 mg/dL; normal value, 60–108 mg/dL), and decreased albumin level (3.3 g/dL; normal value, 3.5–5.5 g/dL). The other blood data were within the normal range including glutamic pyruvic transaminase (11 U/L; normal value, 4–44 U/L), glutamic oxaloacetic transaminase, (26 U/L; normal value, 8–38 U/L), HbA1C (5.6%; normal value, 4%–6%), alpha-fetoprotein (AFP, 1.3 ng/mL; normal value < 10 ng/mL), carcinoembryonic antigen (4.1 ng/mL; normal value < 5 ng/mL), hepatitis B surface antigen (HBsAg; 0.2 s/c; normal value < 1 s/c [s/c = signal per cutoff ratio]), and anti-hepatitis C virus antibody (0.1 s/c; normal value < 0.8 s/c). Ultrasonography (US) of the abdomen revealed a small hyperechoic nodule in the dependent site of the gallbladder, associated with gallbladder distension and wall thickening. The liver showed coarse parenchymal texture, small size, and undulated surface. Additionally, a 5.1 cm, lobulated mass of mixed echogenicity in S6 of the liver was observed; increased blood flow was found inside the mass on color Doppler imaging (images not shown). Cholelithiasis, acute cholecystitis, liver cirrhosis, and liver tumor, especially hepatocellular carcinoma, were suspected based on the US findings. Computed tomography (CT) of the chest and abdomen with and without intravenous contrast administration, including arterial and portal venous phases, was performed. Distension and minimal wall thickening of the gallbladder, and calcified nodules inside the gallbladder were noted, which were compatible with cholelithiasis and acute cholecystitis. On CT also, irregular liver surface and coarse liver parenchyma were identified; a 5.1 cm, lobulated, hypodense, and heterogeneously hypervascular mass was identified in S6 of the liver, showing an early washout pattern and delayed rim enhancement on the portal venous phase. These findings were consistent with liver cirrhosis and associated HCC (Fig. 2). The patient had Child-Pugh class A liver cirrhosis with a score of 6. The liver tumor was classified as stage B in accordance with the Barcelona Clinic Liver Cancer (BCLC) staging system.

Another 11 cm, irregular, and lobulated mass was found in the subareolar region of the left breast. The mass showed interior septation, with solid and fluid components, fluid-hyperdense fluid component level, and enhancement of the solid component after intravenous contrast administration (Fig. 3); overlying skin showed involvement. Therefore, the left breast tumor was suspected to be a clinical stage IIIB tumor (cT4bN0MX) in accordance with the American Joint Committee on Cancer (AJCC) guidelines.

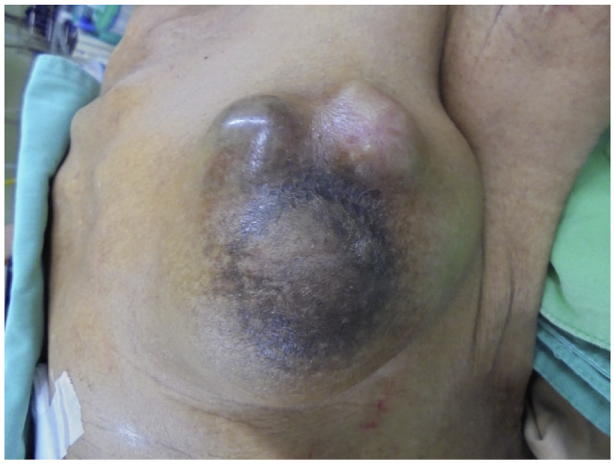

Fig. 1. A large, protruding, lobulated, and hard mass with skin discoloration was found in the left breast area.

US-guided biopsy of the liver mass was performed. The surgeon performed laparoscopic cholecystectomy the next day, along with the removal of an intraperitoneal hematoma caused by the US-guided liver tumor biopsy, and excision of the left breast mass.

On gross examination of the breast mass specimen, it was found to be 13 × 10 × 6 cm^3. The cut surface was friable and grayish-white in color, and much yellowish fluid was observed in the mass. On hematoxylin and eosin (HE) staining, the tumor mass showed prominent trabecular structures and solid cell nests (Fig. 4). The immunohistochemical (IHC) studies revealed strong positive staining for estrogen receptor (ER) and progesterone receptor (PR), but showed negative results for human epidermal growth factor receptor 2 (HER2), AFP, HBsAg, and thyroid transcription factor 1 (TTF-1) staining. Therefore, infiltrating ductal carcinoma not otherwise specified, with predominantly cystic degeneration, was pathologically diagnosed. The pathological findings of the liver biopsy specimen revealed moderately differentiated HCC. The surgeon recommended a second operation of the left breast and dissection of left axillary lymph node (i.e., left modified radical mastectomy); however, the patient refused. The patient then underwent treatment with tamoxifen for the breast cancer and transarterial chemoembolization for the HCC after the operation. The condition of the patient remained stable at the time of the case report.

3. Discussion

Male breast cancer is rare, accounting for approximately 1% of all breast cancers, and has an incidence of only 0.7 per 100,000 population.[1–4] It constitutes only 0.2% of all cases of male cancers.[1] Although the natural history of male breast cancer is similar to that of the female counterpart, the majority of male patients with breast cancer are about 10 years older than female patients with breast cancer,[1,3] and male breast cancer shows a higher level of hormone receptor (ER and PR) expression than the female breast cancer.[3]

Positive family history is a predisposing factor for male breast cancer. Other risk factors for the development of breast cancer in male patients include genetic and hormonal etiologies. The genetic factors include Klinefelter syndrome and mutations of the *BRCA1* and *BRCA2* genes (which are associated with a high risk of breast and ovarian cancers). The hormonal factors for male breast cancer are found in sporadic cases, and consist of obesity, alcohol ingestion, gynecomastia, liver cirrhosis, and lack of exercise.[4–6] Such sporadic breast cancer is related to high levels of circulating estrogens, which stimulate breast growth and play a role in carcinogenesis through the metabolites of estrogen.[4] Although blood estrogen levels were not examined in the present case, the strong positive staining for ER on IHC may suggest that this case of male breast cancer is most likely a sporadic disease.

Alcoholic liver cirrhosis shows an abnormality in the metabolism of sex hormones and leads to a decrease in the circulating androgen levels and a rise in the circulating estrogen levels.[1,7] The resulting hyperestrogenism may be associated with gynecomastia and cholelithiasis, and may play a key role in the development of breast cancer in men.[4–6] Upon chronic alcohol ingestion, ethanol decreases the plasma levels of testosterone by increasing levels of sex hormone-binding globulin, and enhances the metabolism of the estradiol to catechol estrogens, which may be related with the carcinogenesis of breast cancer in a male patient with alcoholic

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