

Case Report

A Case of Hyperintense Liver Metastases of Breast Cancer in the Hepatobiliary Phase on Gadoteric Acid-Enhanced Magnetic Resonance Imaging

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Keywords

Breast cancer · Gadoteric acid-enhanced MRI · Hyperintense liver metastasis · Lymphatic liver metastasis

Abstract

A 64-year-old woman complaining of left arm and breast edema was referred to our hospital. Mammography and ultrasound could not initially show any masses, but magnetic resonance imaging (MRI) showed ill-defined small masses in her left breast. Histological examination showed the tumor to be triple-negative breast cancer. After neoadjuvant chemotherapy, the patient underwent operation. Postoperative histological examination showed massive cancer remnants in the lymph nodes and lymphatics. Enhanced CT taken at the onset of abdominal pain showed multiple liver masses with ring enhancement 17 months after the operation. Gadoteric acid-enhanced MRI showed hyperintense masses and presumed broad cancer cell permeation to the liver in the hepatobiliary phase. Due to the histologically proven high lymphatic permeability, metastatic sites, and gadoteric acid-enhanced MRI findings, we judged the liver metastases as lymphatic liver metastases. Due to the marked liver dysfunction at the onset of abdominal pain, the patient received best supportive care and died in 4 months.

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Introduction

Breast cancer is the most commonly occurring cancer in women in many countries. Due to the prevalence of screening mammography and the advent of various effective new drugs, the mortality rate with breast cancer has already decreased in some Western countries [1, 2]. Breast cancer, however, often metastasizes to the bone, lung, pleura, brain, and liver.

Unlike bone metastasis and brain metastasis, liver metastasis of breast cancer rarely presents with any symptoms until liver function deteriorates beyond a certain threshold. In addition, cure of liver metastasis of breast cancer is generally regarded as exceptional. However, some metastatic, especially so-called oligometastatic, breast cancers with high chemosensitivity have come to show long-term complete response and sometimes presumed cure to the chemotherapy administered, especially with newly developed effective anticancer drugs such as bevacizumab [3] and anti-human epidermal growth factor receptor type 2 agent(s) [4]. Therefore, how should we check up that liver metastasis has not yet been established?

Plain images by computed tomography (CT) and magnetic resonance imaging (MRI) depict the configuration of organs and target lesions on one hand, and enhanced images using contrast media usually disclose the blood flow in the area of interest on the other hand. Gadoteric acid-enhanced MRI [5, 6], like gadoteridol-enhanced MRI, makes blood flow in the target area/lesion(s) clear in the early phase, and around 50% of gadoteric acid is taken up by hepatocytes in the hepatobiliary phase [7]. Metastatic liver tumors, therefore, are usually detected as hypointense masses in the hepatobiliary phase of gadoteric acid-enhanced MRI due to the absence of hepatocytes in the metastatic foci with a generally expansive growth pattern.

We herein describe an extremely rare case of hyperintense liver metastases of breast cancer in the hepatobiliary phase on gadoteric acid-enhanced MRI.

Case Report

A 64-year-old woman with edema in her left arm and left breast was referred to our hospital. Mammography showed neither masses nor presumed malignant calcifications in the breasts. Ultrasound showed breast skin thickening and axillar lymph node swelling without breast tumors. We then judged the edema and lymph node swelling to be caused by some kind of inflammation and initially treated the patient with the antibiotic cefdinir, which resulted in no improvement of the edema. MRI, taken in order to further examine the edema, showed ill-defined small masses with early enhancement in her left upper and outer quadrant of the breast and lymph node swelling in the left axilla. Second-look ultrasound showed obscured small masses in the left breast. Histological examination showed the tumor to be estrogen receptor-, progesterone receptor-, and human epidermal growth factor receptor type 2-negative atypical cells with ovoid nuclei, leading to the diagnosis of triple-negative invasive ductal carcinoma (Fig. 1a). Punch biopsy of the skin showed massive cancer cells in the skin lymphatics. The patient received 4 courses of FEC100 (fluorouracil 500 mg/m², epirubicin 100 mg/m², and cyclophosphamide 500 mg/m² q3w) chemotherapy, followed by 4 courses of docetaxel (75 mg/m² q3w) chemotherapy. After neoadjuvant chemotherapy, the patient underwent mastectomy and axillary dissection. Due both to the viable lymph nodes being resected and the massive cancer remnants in the lymphatics (Fig. 1b), we further treated the patient with post-mastectomy radiotherapy to the chest wall and supraclavicular lymph nodes, followed by adjuvant capecitabine therapy (2,400 mg/day 3 weeks on, 1 week off) [8].

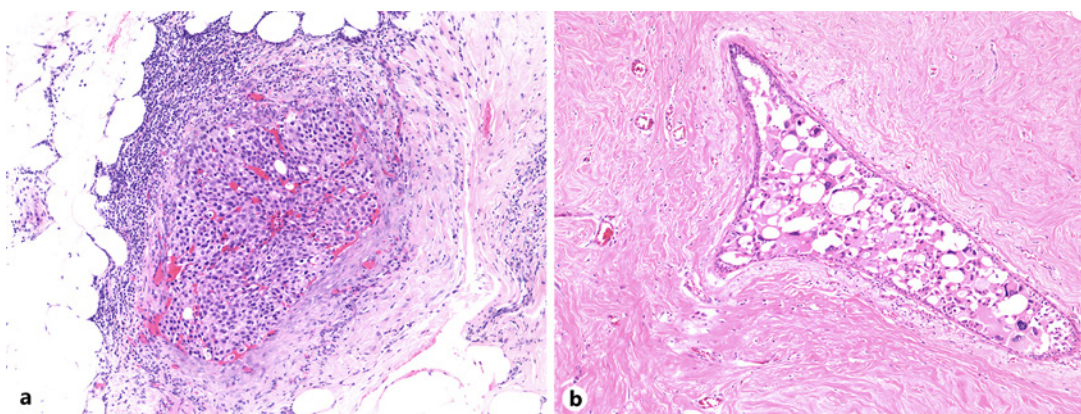


Fig. 1. Pathological examination. **a** Histological examination before neoadjuvant chemotherapy showed invasive ductal carcinoma. HE. $\times 100$. **b** Histological examination showed massive cancer remnants in the lymphatics surrounded by marked fibrosis due to the neoadjuvant chemotherapy. HE. $\times 200$.

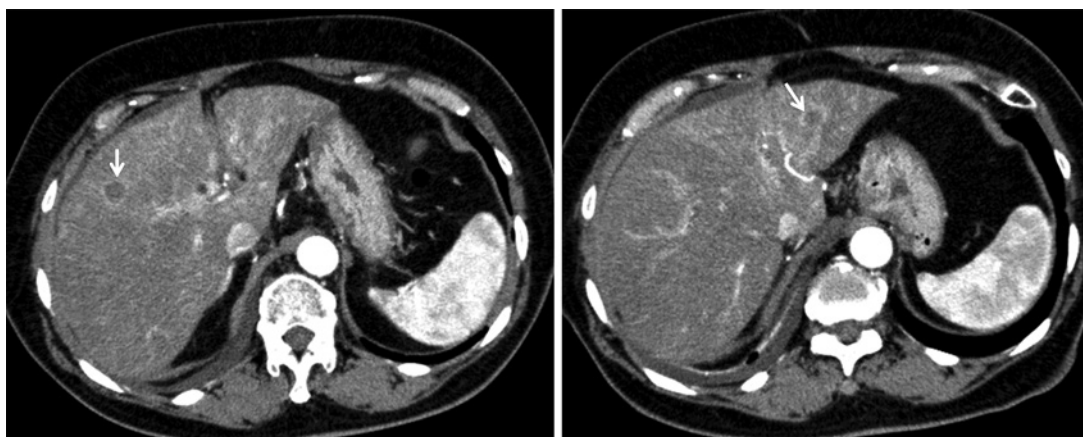


Fig. 2. Computed tomography. Enhanced CT showed small nodules (arrows) with ring enhancement, suggesting metastatic liver tumors.

Follow-up plain CT, taken 12 months after the operation, showed no abnormalities in the lung and liver. Five months later, still on capecitabine therapy, the patient suddenly complained of abdominal pain. Ultrasound showed masses in the liver. Enhanced CT showed small masses with ring enhancement and faint stains in the anterior and superior portion of the liver (Fig. 2).

MRI using gadoxetic acid showed very small masses with hypointensity in the early phase (Fig. 3a, b) and hyperintense and clearly demarcated small lesions in sections 4 and 8 of the liver with diffuse and mixed hyper- and somewhat hypointense stains in the anterior and superior portions of the liver in the hepatobiliary phase (Fig. 3c, d). The presumed affected area was judged as broader on hepatobiliary-phase images by gadoxetic acid-enhanced MRI than on enhanced CT images and on early-phase images by gadoxetic acid-enhanced MRI. Although we did not perform any biopsy of the liver lesions, we judged the liver lesions to be metastases of breast cancer. Due to the simultaneous marked liver dysfunction at the onset of abdominal pain, the patient received best supportive care without further chemotherapy and died within 4 months.

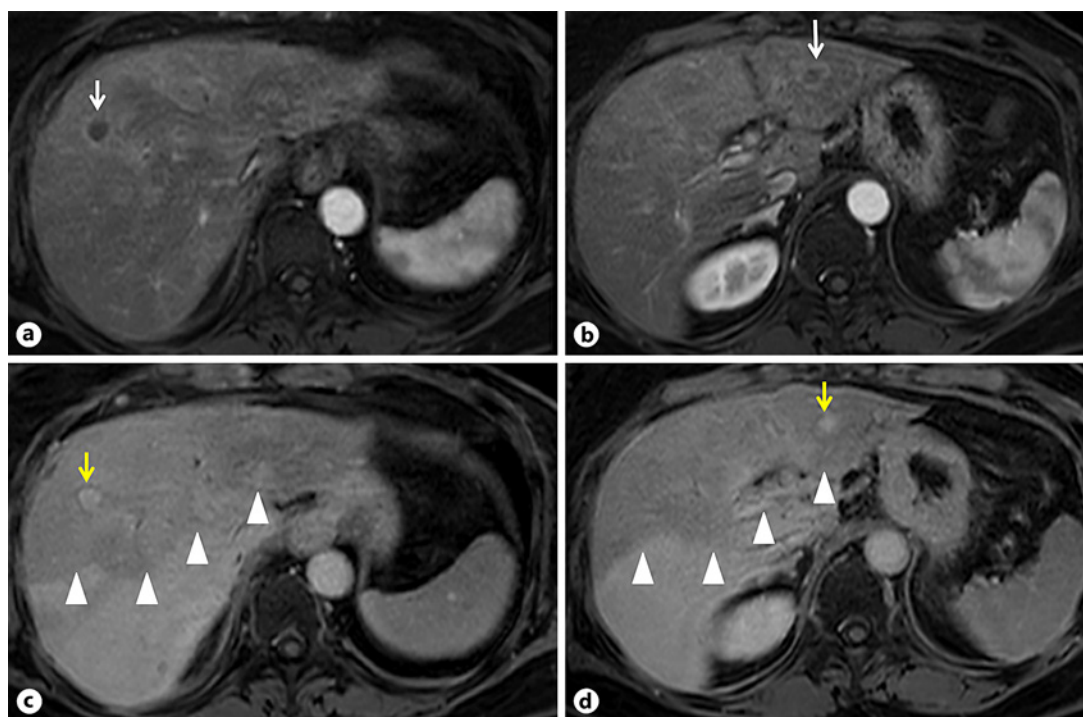


Fig. 3. Gadoxetic acid-enhanced MRI of the liver. Gadoxetic acid-enhanced MRI showed hypointense masses (white arrows) in the early phase (**a, b**) and well-demarcated hyperintense masses (yellow arrows) with presumed diffuse lymphatic permeation to the liver (demarcated by triangles) in the hepatobiliary phase (**c, d**).

Discussion

All malignant tumors have some kind of etiology and need angiogenesis to grow, suggesting enhancement by contrast media both on CT and on MRI. In the diagnosis of breast cancer, MRI using a gadolinium-based contrast agent typically shows strong enhancement in the early phase and a rapid decrease in the following phases. The degree of enhancement depends on the vascularity of and around the tumor. In fact, enhanced CT in our case showed liver tumors with ring enhancement, clearly suggesting metastatic liver tumors.

Gadoxetic acid, like extracellular-type gadolinium-based contrast agents, has vascularity-expressing properties in the early phase but remains in hepatocytes in the hepatobiliary phase, exclusively showing metastatic liver tumors as hypointense masses. In our case, very small tumors in sections 4 and 8 showed hyperintense masses with mixed hyper- and somewhat hypointense stains of the liver parenchyma. A hyperintense area in hepatobiliary-phase images by gadoxetic acid-enhanced MRI implies the presence of Kupffer cells [9], suggesting at least a coexistence of metastatic cancer cells and normal hepatocytes. We further judged that the hepatobiliary-phase images by gadoxetic acid-enhanced MRI clearly indicated a broad area of the anterior and superior portions of the liver to be affected by cancer cells, which explained well the marked liver dysfunction in this case.

Breast cancer generally spreads to the liver hematogenously, leading to multiple and expansive metastases. Due to the lack of histological examination of the liver lesions, we can only speculate that the breast cancer cells metastasized to the liver not hematogenously but lymphogenously in this case, for the following reasons. It is well known that breast cancer can spread to the liver through the lymphatics accompanying the branches of the superior epigastric vessels and falciform ligament [10]. This pathway usually pours into the anterior

and superior portions of the liver, unquestionably corresponding to the liver lesions in our case. In addition, if breast cancer cells had spread hematogenously to the liver in this case, it should have been unlikely that breast cancer cells broadly metastasized only to the area just around the attachment of the falciform ligament to the liver and caused marked liver dysfunction without large and multiple mass formation.

Inflammatory breast cancer is characterized by erythema of the mammary skin with no palpable masses in the breast [11]. The present case lacked mammary skin erythema but presented with skin edema of the left breast, massive axillary lymph node metastases, and very small cancers in the left breast. This strong lymphatic permeability presumably caused lymphatic liver spread. A plain CT scan taken just 5 months before the onset of abdominal pain showed no abnormality. Even if positron emission tomography/enhanced CT had been applied in this case, judged by the enhanced CT findings at the time of abdominal pain, positron emission tomography/CT might also have failed to detect the liver metastases, due to the presumed sparse cancer cell distribution in the liver. Therefore, gadoteric acid-enhanced MRI of the liver should be included in the postoperative follow-up scheme of breast cancer with high lymphatic permeability.

In conclusion, we presented our experience with presumed lymphatic liver metastases of breast cancer showing extremely rare hyperintense liver tumors in the hepatobiliary phase by gadoteric acid-enhanced MRI.

Statement of Ethics

We have reported this case in compliance with the Declaration of Helsinki. Written informed consent was obtained from the family of the deceased patient for the publication of the clinical data.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

T.Y. contributed the design of the report and collected the data. S.O. drafted the manuscript, and M.H. and S.M. revised the manuscript. All authors have read and approved the final version of the manuscript.

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