

Case Report

Liver Metastasis Occurring within Four Months of Early Breast Cancer Diagnosis: A Case Report and Literature Review

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Keywords

Breast cancer · Liver metastasis · Luminal B type · Case report · Follow-up

Abstract

Liver metastasis commonly occurs; however, the luminal-type liver metastasis rarely develops at the early stage of breast cancer, posing key challenges in screening patients, giving early targeted treatment, and providing an opportunity to prolong survival. A 44-year-old female was diagnosed with breast cancer (pT2N0M0, IIa) and luminal B type postoperatively. The latest guidelines indicated four cycles of albumin-paclitaxel and cyclophosphamide chemotherapy. After 4 months of treatment, the patient was found to have hypoechoic nodules in the liver due to other diseases and was thereby diagnosed with breast cancer with liver metastasis. The latest guidelines did not recommend routine imaging and hematological examination of asymptomatic early breast cancer during follow-up. We suggest that follow-up should be strengthened for high-risk patients to maximize their benefits from early diagnosis and treatment.

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Introduction

The current global cancer burden data released by the World Health Organization's International Agency for Research on Cancer in 2020 revealed that the number of new breast cancer cases worldwide in 2020 was as high as 2.26 million, exceeding the 2.2 million

lung cancer cases; breast cancer has therefore surpassed lung cancer as the world's most common cancer [1]. Liver metastasis occurs in about 50% of patients with metastatic breast cancer, whereas 5–12% of patients with liver metastases have a liver recurrence. The prognosis is poor following the liver metastasis, with a median survival rate of only 2–3 years if treated, whereas the overall survival time is 4–8 months without intervention [2, 3]. Therefore, liver metastasis is one of the leading causes of death in patients with advanced breast cancer.

The patient in this case report was classified as stage IIa with luminal B type and received four cycles of paclitaxel (albumin bound) and cyclophosphamide chemotherapy based on the latest Chinese Society of Clinical Oncology and National Comprehensive Cancer Network (NCCN) guidelines. At 4 months post-treatment, the patient showed liver hypoechoic nodules, confirmed as breast cancer metastasis by biopsy. Molecular typing demonstrated hormone receptor (HR)+/human epidermal growth factor receptor 2 (HER2)–. Since liver metastasis is an important factor in the long-term survival of patients with breast cancer, early identification may provide an opportunity for radical hepatectomy and prolonged survival [2]. This case report with a review of relevant literature is presented following the CARE reporting checklist.

Case Presentation

A 44-year-old woman presented to the Department of Breast Surgery (Qingdao Municipal Hospital, Shandong, China) due to a breast mass detected 1 week before the presentation. She was previously healthy and stated that she was not presently menopausal and did not have a family history of breast cancer. At postadministration, a 3 × 4-cm tumor was palpated above the left breast areola area. No axillary or supraclavicular lymph node metastasis was detected. Laboratory tests showed that liver function and some blood tumor markers were within the normal ranges; however, cancer antigen-153 (Ca-153) was slightly elevated. Cardiac ultrasound (US), gynecological US, cranial computed tomography (CT), chest CT, abdominal CT, and the bone scan did not reveal any irregular findings.

The punctured tissue in the left breast was found to be an invasive carcinoma. At post-consultation, mastectomy and sentinel lymph node biopsy were performed. Postoperative pathology indicated that the invasive ductal carcinoma size was 3.5 × 3 × 3 cm, the histological grade was III, presence of vascular and nerve invasion, and five sentinel lymph nodes without tumor invasion. Immunohistochemistry results were as follows: estrogen receptor (ER) (70%++), progesterone receptor (PR) (90%+++), HER-2 (0), KI67 (about 30%+), and programmed death-ligand 1 (SP142; about 3%), diagnosed as pT2N0M0, IIa, and luminal B type.

The latest Chinese Society of Clinical Oncology and NCCN guidelines indicated the treatment regimens were four cycles of chemotherapy and 5 years of endocrine therapy without ovarian function suppression. At 2 weeks postoperatively, the patient was administered albumin-paclitaxel 260 mg/m² and cyclophosphamide 600 mg/m² on day 1 in a 21-day cycle for four cycles. The patient underwent chest CT due to other diseases (Fig. 1), suggesting the presence of abnormal echoic nodules in the liver 4 months after breast cancer treatment. Magnetic resonance imaging showed rounded masses (Fig. 2). Diffusion-weighted imaging showed a high signal and clear boundary; the largest mass was located in the left lobe of the liver with a diameter of approximately 2.9 cm. US imaging suggested multiple low-echo nodules in the liver (Fig. 2). Liver tumor biopsy indicated ER (>90%++), PR (>90%++), GATA3 (+), HER-2 (1+), and KI67 (about 10%+), which were consistent with adipogenic carcinoma and confirmed liver metastasis from breast cancer. Multidisciplinary

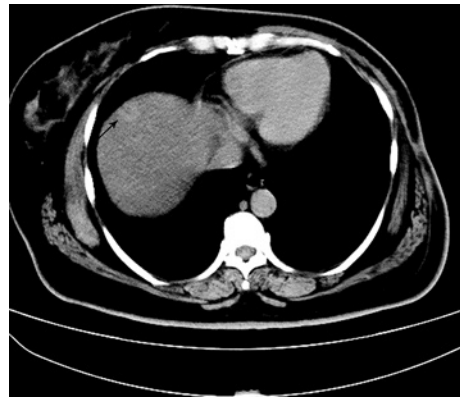


Fig. 1. There is an abnormal echoic nodule about 1.5 cm in the right lobe of liver.

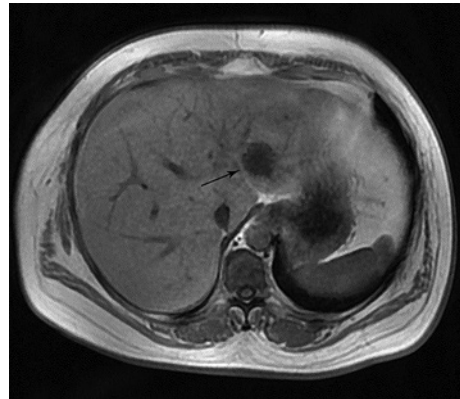


Fig. 2. Largest metastatic lesion in the left lobe of the liver was 2.9 cm in diameter and showed a high DWI signal, diffusion-weighted imaging.

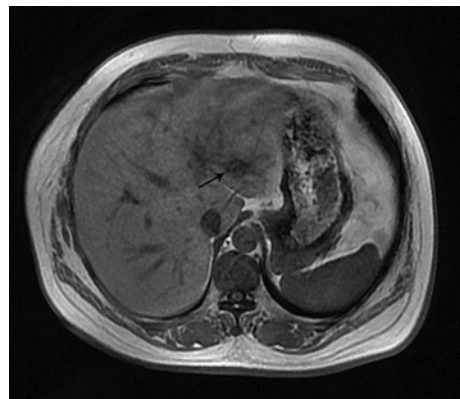


Fig. 3. Metastatic lesion in the lobe of the liver was 2.0 cm in diameter after treatment.

discussions (breast surgery, oncology, radiology, interventional surgery, hepatobiliary surgery, US, and pathology department) determined the subsequent treatment plans as follows: ovarian function suppression, goserelin (3.6 mg i.v., every 28 days), an aromatase inhibitor (anastrozole 1 mg daily), and a CDK 4/6 inhibitor (abemaciclib 150 mg twice a day); considering that the patient was a young woman with liver metastasis, genetic testing was suggested, but the patient refused; liver lesions shrunk below their pretreatment sizes after 4 months (Fig. 3).

Discussion

The liver is the third most common site of metastasis in patients with breast cancer. The incidence of liver metastasis at the first site varies from 17.8% to 35% [4]. Breast cancer is associated with spatial and temporal heterogeneity of specific molecular subtypes. Each subtype has a clear pattern of organ-specific metastasis and colonization. Therefore, among different molecular breast cancer types, HER2+, namely, ER–/PR–/HER2+ (HR–/HER2+) liver metastasis, has the highest incidence, accounting for 4.6% of all patients, whereas patients with HR+/HER2– have the lowest possibility of recurrence and liver metastasis, and its incidence is four times lower than that of HER2 (+) malignant tumors [5].

Duan et al. [6] reported the time to liver metastasis (TTLM) significantly varies among different breast cancer types. Triple-negative breast cancer has the shortest TTLM of 15 months, followed by 21 months in patients with HR–/HER2+, whereas the TTLM is 30 months for patients with HR+/HER2– and 34 months for patients with HR+/HER2+. Among all patients with metastatic disease, 48.8% presented stage II disease, and 13 patients (10.6%) developed the metastatic disease within 1 year, including only two (4.1%) with HR+/HER2–. In the report by Sadot et al [7], the median time interval of TTLM was 42 months, and the shortest time was 16 months. Among these patients with metastases, 66% were lymph node-negative, 97% were ER-positive, and 78% were PR-positive.

When liver metastases are small, patients are usually asymptomatic, and metastases can only be detected in imaging studies. Due to more effective treatment and better tolerance at early stages, early detection of liver metastases seems to result in better outcomes for specific patients [5]. However, in the National Surgical Adjuvant Breast and Bowel Project B-09 study [8], 7,984 bone scans were performed during the follow-up of 2,697 patients, and only one asymptomatic patient (0.6%) was found to have bone metastasis. Hanib et al. [9] found no metastasis in asymptomatic patients during the follow-up of 273 patients. Tanaka et al. [10] reported that only 1% of asymptomatic (stage I and II) patients were diagnosed with distant metastasis on enhanced CT during follow-up of 483 asymptomatic patients. Although circulating tumor markers can be used during follow-up to identify distant metastases in asymptomatic patients, they were not recommended by most US and European experts due to the absence of high-level evidence [11]. The NCCN and European Society for Medical Oncology do not recommend CT, magnetic resonance imaging, US, or positron emission tomography/CT in asymptomatic patients in stages 0–II, even in those with lymph node metastasis, to identify distant metastasis [11, 12]. Therefore, experts recommend a higher level examination used only if there are obvious symptoms or signs.

When intrahepatic metastasis is suspected, biopsy helps re-evaluate the ER, PR, HER-2, Karnofsky Performance Score, Ki-67, grade, and other indicators to determine a more effective treatment strategy for patients with liver metastasis. In this patient, liver metastasis was found during an examination for other diseases but without obvious clinical symptoms. After the puncture, the diagnosis of breast cancer was confirmed. Possible reasons are as follows: first, the postoperative pathological examination of the patient indicated grade III histology, vascular invasion (+), nerve invasion (+), and KI67 (approximately 30%+). The Breast International Group Trial 1–98 showed that a higher Ki-67 labeling index was associated with adverse prognostic factors and with worse disease-free survival [13]. The histological grade was closely associated with multiple liver metastases [14]. The larger tumor size may be associated with a slightly higher incidence of central nervous system involvement [15]. Therefore, two points can explain why liver metastasis occurred early in this patient. First, with multiple risk factors, cancer cells can spread to the other organ through the lymphatic

or hematological system. Second, patients are insensitive or even resistant to chemotherapy, resulting in ineffective treatment. Therefore, follow-up should be strengthened for these patients with multiple risk factors for the early detection of metastasis, who benefited from more effective treatment, resulting in prolonged survival.

To date, international guidelines recommend endocrine therapy as the first choice for patients with HR+/HER2– metastatic breast cancer, except for life-threatening metastatic diseases requiring rapid control [12]. In addition to systemic treatment, other treatment options are local surgical resection, stereotactic body radiation therapy, percutaneous thermal ablation, and segmental resection after the occurrence of liver metastasis of breast cancer. Nowadays, surgery for liver metastases has shown partial benefits; however, no consensus has been established on the optimal timing of liver metastases and the number and diameter of liver metastases suitable for surgical resection, requiring more prospective randomized controlled studies. The efficacy of thermal ablation and radiotherapy for the treatment of breast cancer liver metastasis remains controversial.

Conclusion

Liver metastases from breast cancer are common; however, liver metastasis is less common in patients with HR+/HER2–. This case suggests that for asymptomatic patients with early breast cancer, if there are multiple risk factors, especially vascular invasion, their follow-up management should be strengthened to detect metastasis at an early stage. After suspecting liver metastasis, a needle biopsy is recommended to make an accurate treatment plan. For HR+/HER-2 metastatic disease without visceral crisis, endocrine therapy should first be performed.

Statement of Ethics

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. Ethical approval is not required for this case report in accordance with local or national guidelines.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Data collection and assembly: Jing Jing Yuan and Jie Jiang. Data interpretation and manuscript writing: Zhi Xu and Lei Ma. Revising the work critically for intellectual content: Zhi Xu, Lei Ma, and Jing Jing Yuan. All the authors approved the final manuscript and agree to be accountable for all aspects of the work.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the first author Zhi Xu.

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