Prolonged Progression-Free Survival in a Patient With Triple-Negative Breast Cancer Metastatic to the Liver After Chemotherapy and Local Radiation Therapy

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Clinical Practice Points

- Patients with triple-negative metastatic breast cancer (negative for estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2) that progresses after standard systemic chemotherapy have limited treatment options and a poor prognosis.
- This report presents the case of a 50-year-old woman with triple-negative breast cancer with liver-only metastases who achieved extended progression-free survival off systemic chemotherapy for approximately 3 years after initial treatment with chemotherapy and precision radiotherapy to her liver metastases.

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Introduction

Triple-negative breast cancer (TNBC) is a histopathologic diagnosis based on the absence of expression of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2, ERBB2) ($ER^-/PR^-/HER2^-$).[1] TNBC is associated with a worse prognosis compared with hormone receptor–positive (HR^+) tumors. A prospective study by Lin et al[2] of 15,204 women between January 2000 and December 2006 found that patients with TNBC had worse breast cancer–specific and overall survival, even after adjusting for various confounding factors. However, TNBC is associated with considerable heterogeneity with respect to clinical outcomes.[3]

Approximately half of the patients with metastatic breast cancer will develop liver metastases, which are typically associated with a state of widely disseminated disease and involvement of other visceral organs.[4] The prognosis of patients with liver or lung metastases is generally inferior to that of patients with bone metastases.[4] However, a minority of patients (about 5%) with stage IV breast cancer present with liver-only metastases.[5] The prognosis of patients with liver-only metastases may be better than that of patients who have liver metastases and widespread disease.[6]

This report presents the case of a 50-year-old woman with a diagnosis of TNBC metastatic to the liver who achieved extended progression-free survival after systemic chemotherapy and precision radiotherapy to liver metastases.

Case Report

In August of 2006, a 50-year-old white woman with no medical history or family history of breast cancer palpated a mass in the inferior aspect of her right breast. A mammogram found a 2-cm suspicious mass at the 6-o'clock position, and an ultrasound confirmed the presence of an irregular lobular cystic mass. A fine-needle aspiration was nondiagnostic, and she therefore underwent an excisional biopsy of the right breast in September of 2006, which found a 3.5 × 2.0 × 1.5-cm poorly differentiated infiltrating ductal carcinoma, nuclear grade 3 with necrosis. There was no evidence of lymphovascular invasion. There was also ductal carcinoma in situ, grade III. The invasive tumor was ER^-/PR^-. There was no HER2 overexpression by immunohistochemistry (score 0), and HER2 gene amplification was not identified by fluorescent in situ hybridization assay; the ratio of HER2 to chromosome 17 centromere (CEP17) was 1.0. The surgical margins were positive at the inked portion of the resected specimen. She underwent genetic testing, which found no evidence of breast cancer 1 or 2 early onset gene (*BRCA1* or *BRCA2*) mutations. Baseline radiographic staging with a computed

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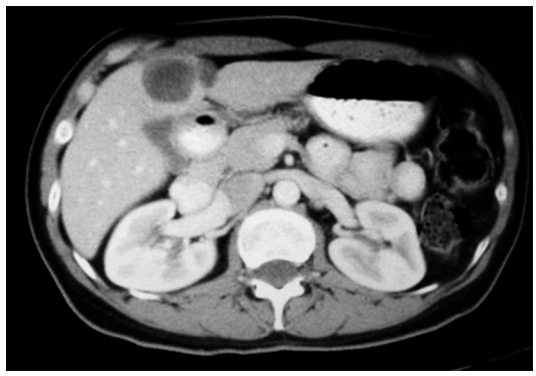
tomography scan of the chest, abdomen, and pelvis (CT C/A/P) in September 2006 found 3 hypodense, enhancing liver lesions consistent in appearance with metastases, ranging in size up to 2.3 cm (Fig. 1). This was confirmed by a subsequent magnetic resonance imaging (MRI) study of the abdomen. A bone scan found no skeletal metastases.

After the diagnosis of metastatic disease, she was started on systemic chemotherapy with weekly paclitaxel at a dose of 80 mg/m^2 in October 2006, and later bevacizumab at 10 mg/kg was added. While on treatment, she developed a palpable mass at the surgical site in the right breast that grew to a size of 5.6 cm over 2 months (Fig. 2). A biopsy in December of 2006 found a poorly differentiated infiltrating ductal carcinoma, nuclear grade 3, which was similar to her original tumor pathology. The tumor was ER$^-$/PR$^-$. HER2$^-$ status was determined by immunohistochemistry (score 1+), and HER2 gene amplification was not identified by fluorescent in situ hybridization assay (HER2:CEP17 ratio, 1.18). A positron emission tomography–computed tomography scan in December 2006 found increased fluorine-18 fluorodeoxyglucose (FDG) activity in the breast mass (standardized uptake value [SUV], 20.2), the largest liver mass (SUV, 13.0), and FDG activity in a lesion of the right lobe of the liver that had an SUV of 3.9. She enrolled in a clinical trial and was treated with an mTOR inhibitor–containing regimen. After receiving approximately 6 weeks of therapy, she had an increase in the size of the right breast mass. This was confirmed on a CT scan, with the breast mass increasing from 5.6 cm to 8.3 cm in diameter when compared with the pretreatment study. There was also interval increase in the metastatic burden of the liver. Given the concern for the rapid disease progression, doxorubicin at 60 mg/m^2 and cyclophosphamide at 600 mg/m^2 were administered, and she received 5 cycles with clinical and radiographic response. Subsequently, in April 2007, treatment was changed to weekly single-agent vinorelbine at 25 mg/m^2. A follow-up CT C/A/P obtained in December 2007 found resolution of the right breast mass (Fig. 3A) and shrinkage of the hepatic metastases (see Fig. 3B). Vinorelbine was continued until February 2010 for a total of 33 cycles, with good clinical and radiographic response, and she tolerated this regimen quite well. Restaging CT C/A/P in February 2010 found a residual 5-mm left hepatic lobe lesion. A mammogram found benign calcifications with no residual mass in her breast. As a result of the sustained excellent radiographic response of her breast and liver lesions to systemic chemotherapy, the patient was offered a chemotherapy holiday.

The patient then expressed interest in local therapies for the breast and liver. Options including surgery, radiation therapy, and radiofrequency ablation were discussed with the patient, and she elected to pursue radiation therapy. In March 2010, she underwent simulation for the liver lesion, using full-body vacuum bag immobilization with rigid abdominal compression and shallow breathing. A gadoxetate (Eovist)-enhanced treatment-planning MRI scan of the liver was obtained that found only a single 0.5-cm residual tumor nodule, and this was merged with the treatment-planning CT for target definition. Because the tumor was adjacent to the small bowel, a dose of 40 Gy in 10 fractions was chosen to provide a biologically potent treatment while minimizing the risk of toxicity (Fig. 4A, B). The patient tolerated treatment well, with no side effects. She then received a course of 42.5 Gy in 16 fractions to the right breast using standard tangent fields. She developed minimal in-field dermatitis and completed treatment without incident.

Figure 1 Hepatic Metastasis as Seen on Computed Tomography Scan From December 2006



She continued to be followed up clinically and radiographically. A CT C/A/P from May 2012 found no evidence of disease. There was a mild hypodensity along the fissure for the ligamentum teres, which was benign. This was in the area of the prior high-dose liver radiation. A mammogram from September 2012 found only postoperative changes in the right breast.

The most recent bone scan and CT C/A/P in May 2013 found no evidence of metastatic disease. Laboratory studies done at the time found normal blood counts, liver function test results, and creatinine levels. Measurements of carcinoma antigens CA 27-29 and CA 15-3 and of carcinoembryonic antigen have been unremarkable.

Discussion

The median overall survival of patients with metastatic breast cancer ranges from 18 to 24 months.[7] The overall survival of patients with metastatic TNBC is reported to be worse when compared with patients with HR$^+$ breast cancer. A retrospective study of 3726 breast cancer patients found a median survival of only 6 to 11 months for patients with metastatic triple-negative tumors.[8]

Figure 2 Biopsy-Proven Right Breast Recurrence as Seen on Computed Tomography Scan From December 2006