Case Report

Evaluation of treatment response for breast cancer: are we entering the era of "biological complete remission"?

Li Bian[1], Tao Wang[1], Yi Liu[2], Hui-Qiang Zhang[1], Jin-Jie Song[1], Shao-Hua Zhang[1], Shi-Kai Wu[1], San-Tai Song[1], Ze-Fei Jiang[1]

[1]Department of Breast Cancer, Affiliated Hospital of Academy of Military Medical Sciences, Beijing, China; [2]Laboratory of Oncology, Affiliated Hospital of Academy of Military Medical Sciences, Beijing, China

Corresponding to: Ze-Fei Jiang. Department of Breast Cancer, Affiliated Hospital of Academy of Military Medical Sciences, No.8 Dongda Street, Fengtai District, Beijing, China. Email: jiangzefei@medmail.com.cn.

Abstract: Breast cancer is one of the most common malignancies in women. The post-operative recurrence and metastasis are the leading causes of breast cancer-related mortality. In this study, we tried to explore the role of circulating tumor cell (CTC) detection combination PET/CT technology evaluating the prognosis and treatment response of patients with breast cancer; meanwhile, we attempted to assess the concept of "biological complete remission" (bCR) in this regard. A 56-year-old patient with breast cancer ($T_2N_1M_1$, stage IV left breast cancer, with metastasis to axillary lymph nodes and lungs) received 6 cycles of salvage treatment with albumin-bound paclitaxel plus capecitabine and trastuzumab. Then, she underwent CTC detection and PET/CT for efficacy evaluation. CTC detection combination PET/CT is useful for the evaluation of the biological efficacy of therapies for breast cancer. The bCR of the patient appeared earlier than the conventional clinical imaging complete remission and promised the histological (pathological) complete remission. The integrated application of the concepts including bCR, imageological CR, and histological CR can achieve the early and accurate assessment of biological therapeutic reponse and prognosis of breast cancer.

Key Words: Breast cancer; circulating tumor cell; PET/CT; biological complete remission

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Introduction

Breast cancer is one of the most common malignancies in women. Its incidence has continuously increased, with 1 million new cases annually worldwide. The breast cancer cases accounted for 25-30% of all malignancies in European and American women (1). The incidence of breast cancer grew rapidly in China in the past years. It ranks first in urban areas and fifth in rural areas, and the mortality of breast cancer ranks fourth or fifth among cancer-related mortalities in metropolitan areas. The post-operative recurrence and metastasis are the leading causes of breast cancer-related mortality. Surgery for early breast cancer usually can achieve satisfactory results. The 5-year survival rate for stage I breast cancer can reach 92%, and the 5-year survival rate for stage II breast cancer can be 81% (2). However, most breast cancer cases were identified and confirmed at their late stages and have became surgically unresectable. In some other patients, although their tumors are confirmed at the early stage and show no symptoms of metastasis, tumor metastasis and/or relapse do occur after the resection of the tumor. These results are close related with the occult micrometastases of tumors and the circulating tumor cell (CTC) (3).

The micrometastases originate from the seeding of tumor cells in circulation. Therefore, CTC may be a marker of distant metastasis. In recent years, the development of sensitive molecular biological techniques have made the isolation and counting of peripheral CTC possible.

Table 1 Circulating tumor cell (CTC) detection combination PET/CT technology evaluating the treatment response

	CTC determination (per 7.5 mL peripheral blood)	PET/CT							
		Left breast cancer		Left axillary lymph nodes metastasis		Lung metastasis			
		CT (cm)	SUV_{max}	CT (cm)	SUV_{max}	1	2	3	SUV_{max}
Before treatment (July 27, 2010)	3 (2 $HER2^+$ and 1 $HER2^-$)	2.1	8.3	1.4	2.6	1.9	1.5	1.5	18.6
After one cycle (August 18, 2010) *PR*	0	0.9	1.8	1.1	0.7	1.1	1.0	0.6	1.7
After two cycles (September 8, 2010)		0	1.8	0.6	0	1.1	0.8	0.4	1.3
After three cycles (October 09, 2010) *bCR*	0	0	0	0.5	0	1.0	0.6	0.3	0
After four cycles (October 28, 2010)		0	0	0	0	0.8	0.5	0.3	0
After five cycles (November 23, 2010)		ND							
After six cycles (December 17, 2010)		0	0	0	0	0.8	0.5	0	0

Traditionally, the efficacy of breast cancer treatment is evaluated via imageological methods; however, along with the development of molecular biological technology, the biological efficacy evaluation has shown certain advantages. As shown by research, in the early stage, CTC can be used for the differentiation of benign and malignant tumors and for predicting and judging the risk of metastasis; during the baseline phase before treatment and immediately after treatment, determination of CTC can be used for the early prediction of the treatment efficacy (4,5). Also in recent years, the advances in PET/CT technology has made it possible to identify the residual disease and relapse after treatment, monitor the existence of distant metastasis, and evaluate the treatment response, moreover, PET/CT can detect changes in the tumor metabolism; thus, compared with the conventional imageological techniques, it can reflect the efficacy in an earlier and more accurate manner (5-7).

The combined application of CTC technology and PET/CT technology can realize the "evaluation of biological efficacy" for breast cancer. When evaluating the efficacy of treatment for breast cancer, the concept of "complete remission" (CR) initially includes clinical imaging complete remission and pathological complete remission (pCR). However, along with the optimization of CTC and PET/CT technology, a new concept, biological complete remission (bCR) has emerged in clinical practices. In our depart, the efficacy of treatment for a patient with stage IV breast cancer was evaluated with CTC technology and PET/CT. The data are reported as below.

Case presentation

A 56-year-old woman was presented in our department in July 2010. On physical examination, a 3.5-cm mass was detected in the lower outer quadrant of the left breast. Ultrasound-guided biopsy showed infiltrating ductal carcinoma of the left breast. Immunohistochemistry showed ER(-), PR(-), and HER2(+++). PET/CT indicated left breast cancer accompanied with metastasis to axillary lymph nodes and both lungs. The final diagnosis was T2N1M1, stage IV left breast cancer, with metastasis to axillary lymph nodes and lungs. After the diagnosis was confirmed, chemotherapy was used in combination with Her2 targeted therapy. Since weekly albumin-bound paclitaxel (ABP) has shown higher efficacy in treating metastatic breast cancer than docetaxel, let alone its good safety and patient adherence. The final treatment protocol was ABP (200 mg, 126.6 mg/m^2; d1 and d8) in combination with capecitabine (3,000 mg, 1898.7 mg/m^2, d1-14) and trastuzumab (440 mg, d1). Before treatment and in each 3-week cycle, CTC was determined using CellSearch System (Veridex LLC, Raritan, NJ); meanwhile, the treatment response was evaluated with PET/CT (General Electric Medical Systems, Waukesha, WI). The results are shown in *Table 1*.

Discussion

Albumin-bound paclitaxel (Abraxane) is a new, solvent-free paclitaxel chemotherapy drug. Its outer layer is wrapped in albumin, and its core is paclitaxel nanoparticles that do not dissolve in water. One albumin molecule can be bound with seven paclitaxel molecules. Mediated by the albumin receptor Gp60 and caveolae on the cell membrane, the nanoparticles enter the tumor tissue via the gap junctions in vascular endothelial cells and bind to the secreted protein acidic and rich in cysteine (SPARC) in the tumor interstitium.