Two Cases of Mastectomy after Paclitaxel + Bevacizumab Therapy for Locally Advanced Breast Cancer

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Key Words

Locally advanced breast cancer · Bevacizumab · Paclitaxel

Abstract

Introduction: Locally advanced breast cancer (LABC) deteriorates the quality of life (QOL) of the affected patients. Combination chemotherapy or extended chemotherapy is considered to help to shrink local lesions. **Case 1:** A 71-year-old female with a history of tympanitis and cystitis with methicillin-resistant *Staphylococcus aureus* (MRSA) visited our hospital. There was a tumor of 7 cm in diameter in her right breast with skin ulceration. Paclitaxel + bevacizumab therapy was started, and after five cycles of therapy, a mastectomy with axillary dissection was performed. Chemotherapy with anthracycline was avoided for fear of activating the MRSA. After the operation, the patient's wound opened. However, it naturally epithelialized. **Case 2:** A 41-year-old female visited our hospital due to a tumor of 8 cm in diameter in her right breast with skin ulceration. Four cycles of paclitaxel + bevacizumab therapy were started, and her tumor almost disappeared during the first cycle. Then, doxorubicin + cyclophosphamide therapy was performed for four cycles, and a mastectomy with axillary dissection was performed. Her postoperative course was good. **Discussion:** Chemotherapy with bevacizumab or extended chemotherapy is generally not considered to contribute to a survival improvement. However, such therapy contributes in increasing the response to chemotherapy, and should be considered for patients with LABC to shrink the local lesions and improve the QOL.

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Introduction

Locally advanced breast cancer (LABC) deteriorates the quality of life (QOL) of the affected patients. Systemic therapy with anticancer drugs is usually performed to improve the

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overall survival (OS) or disease-free survival (DFS) when a breast cancer is considered to be a systemic disease. However, chemotherapy for LABC may improve the patient's QOL by shrinking local lesions. Therefore, chemotherapy for LABC should be performed as a local therapy, as well as systemic therapy. In order to shrink a local lesion more efficiently, combining another drug with standard therapy or extending the standard therapy is useful, even when this will not improve the OS or DFS. We herein report two cases of mastectomy after paclitaxel + bevacizumab therapy for LABC.

Case Reports

Case 1

The patient was a 71-year-old female with a history of chronic tympanitis and chronic cystitis with methicillin-resistant *Staphylococcus aureus* (MRSA). She visited our hospital with a chief complaint of a right breast tumor. A tumor measuring 7 cm in diameter in the right upper-outer quadrant of her right breast was observed, with skin ulceration and edema (fig. 1a). Computed tomography (CT) revealed a right breast tumor of 5.5 cm in diameter and axillary lymph node swelling, but there was no apparent distant metastasis (fig. 1a). Bone scintigraphy revealed no abnormal uptake. The results of the blood tests were almost normal, and the levels of tumor markers, such as CEA and CA15–3, were not elevated.

A core needle biopsy was performed, and the pathological diagnosis was invasive ductal carcinoma, which was positive for the estrogen receptor (ER), negative for the progesterone receptor (PgR) and negative for the human EGFR-related protein (HER2). Based on these results, we diagnosed the patient with a locally advanced right breast cancer with no metastatic lesions, and a therapy of paclitaxel combined with bevacizumab therapy was administered.

After five cycles of therapy, the tumor shrunk and became resectable (fig. 2a). Chemotherapy with an anthracycline was avoided to prevent the activation of MRSA, and a mastectomy with axillary lymph node dissection was performed 6 weeks after the last administration of bevacizumab (fig. 2b). Pathological study revealed many viable cancer cells and no change of the ER, PgR and HER2 status (fig. 2c). After the surgery, part of the wound edge became necrotic; however, it naturally epithelialized within 4 weeks (fig. 2d). The patient underwent postmastectomy radiation therapy with a total dose of 50 Gy.

Case 2

The patient was a 41-year-old female with no remarkable medical history. She visited our hospital with a chief complaint of a right breast tumor. The tumor measured 8 cm in diameter and was located in the central portion of her right breast, with skin ulceration and edema. PET/CT revealed a right breast tumor of 6 cm in diameter with axillary lymph node swelling. No apparent distant metastasis was detected. The results of the blood tests were almost normal, and the levels of tumor markers, such as CEA and CA15–3, were not elevated.

A core needle biopsy was performed, and the pathological diagnosis was invasive ductal carcinoma, which was positive for the ER, negative for the PgR and the HER2. A therapy of paclitaxel combined with bevacizumab was performed, and after the drugs had been administered two times, the tumor almost disappeared (fig. 3a). Paclitaxel + bevacizumab therapy was administered for a total of four cycles, and then doxorubicin + cyclophosphamide therapy was performed for four cycles. The site where the tumor had been healed with granulation (fig. 3a), and a mastectomy with axillary lymph node dissection was performed 7 weeks after the last administration of bevacizumab (fig. 3b).

The pathology of the surgical specimen revealed a few viable cancer cells around the scar, and the expression levels of the ER, PgR, and HER2 were greatly decreased (fig. 3c). The patient's postoperative course was good, and she received 50 Gy of postmastectomy radiation therapy.

Discussion

We experienced two cases of LABC that were successfully resected after chemotherapy with paclitaxel + bevacizumab. Here, we defined LABC as breast cancer that is not easy to resect due to the progression of the disease. LABC causes skin ulceration, fluid secretion, bleeding and a bad smell, all of which deteriorate the patients' QOL. According to the guidelines for breast cancer, LABC should be treated with chemotherapy first because it is likely to be a systemic disease [1]. However, patients with LABC often complain of local symptoms, and so treating the local lesions of such patients with chemotherapy is also important. Considering the results of adjuvant chemotherapy for breast cancer, combination therapy or extended chemotherapy may not contribute to an improvement of the OS or DFS [2–4]. However, such treatment can improve the outcome for the patients with LABC, allowing the local lesions to be effectively decreased in size.

Bevacizumab is usually combined with paclitaxel for metastatic breast cancer, and this combination improves the progression-free survival and response rates. However, it does not improve the OS [5]. The BEATRICE trial, which investigated the contribution of bevacizumab as adjuvant therapy for triple negative breast cancer, revealed no efficacy of bevacizumab [6]. These results suggested that bevacizumab could not contribute to the OS in an adjuvant or metastatic setting. There have been several trials that have investigated the efficacy of bevacizumab as preoperative chemotherapy (table 1), and these trials also demonstrated that bevacizumab did not contribute to the OS. However, bevacizumab increased the response rate to chemotherapy [7–11]. There are no data suggesting that bevacizumab deteriorates the patients' OS. Therefore, to control local lesions, using a combination of bevacizumab with standard therapy for LABC as many times as possible seemed to have potential. Bevacizumab has been considered to increase the rate of surgical complications. However, a 4-week interval between the last bevacizumab infusion and surgery appeared to be sufficient to reduce the incidence of therapy-associated surgical complications in a previous study [8].

Basic studies about bevacizumab have suggested that it increases the permeability of vessels around a tumor, and this effect helps the anticancer drug to reach the center of the tumor [12, 13]. This is why chemotherapy with bevacizumab is also effective against large tumors. This combination was therefore indicated for our patients given the large size of their tumors.

In conclusion, extended chemotherapy with bevacizumab for LABC is considered to contribute to improving the patients' QOL, and if possible, resection of the LABC should be performed to help improve or maintain the patients' QOL. Clinical trials investigating such a strategy should be conducted in the future.

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Table 1. Preoperative chemotherapies including bevacizumab

Author or trial	Year	n	Size	Regimen	ORR	pCR
NSABP B-40	2012	1,206	>40 mm	TX ± Bev → AC ± Bev	–Bev 80%	–Bev 28.2%
				TX ± Bev → AC ± Bev	+Bev 87%	+Bev 34.5%
				TG ± Bev → AC ± Bev		
GeparQuint	2012	1,948	40 mm (median)	EC → DTX ± Bev	–Bev 79.2 +Bev 86.8%	–Bev 14.9% +Bev 18.4%
Hurvitz	2008	20	>3 cm	TAC ± Bev	–Bev 90% +Bev 96%	–Bev 63% +Bev 57%
Makhoul	2013	40	58 mm (median)	TC + Bev → A	94%	41%
Kim	2013	45	39 mm (median)	DTX + CBDCA + Bev	96%	42%

Bev = Bevacizumab; TX = docetaxel + capecitabine; AC = doxorubicin + cyclophosphamide; TG = docetaxel + gemcitabine; EC = epirubicin + cyclophosphamide; DTX = docetaxel; TAC = docetaxel + doxorubicin + cyclophosphamide; TC = docetaxel + cyclophosphamide; A = doxorubicin; CBDCA = carboplatin.

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Fig. 1. **a** Images of case 1 (visual examination, CT and bone scintigraphy). **b** Images of case 2 (PET-CT).

Fig. 2. Treatment course of case 1. **a** Visual examination and CT images (pretreatment, after two cycles of PTX + BV and after five cycles of PTX + BV). **b** Resected specimen. **c** The histological findings of the preoperative core needle biopsy (upper) and resected specimen (lower) (HE, ER, PgR, HER2). **d** Open wound and epithelialization after the operation. PTX + BV = Paclitaxel + bevacizumab therapy; AC = doxorubicin + cyclophosphamide therapy.

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Fig. 3. Treatment course of case 2. **a** Visual examination (during the first cycle of PTX + BV, after four cycles of PTX + BV and after four cycles of AC) and CT images (pretreatment, during the first cycle of PTX + BV, after four cycles of PTX + BV and after four cycles of AC). **b** Resected specimen. **c** Histological findings of the preoperative core needle biopsy (upper) and resected specimen (lower) (HE, ER, PgR, HER2). PTX + BV = Paclitaxel + bevacizumab therapy; AC = doxorubicin + cyclophosphamide therapy