

Two Cases with a Long-term Survival Following Multidisciplinary Treatment for Recurrent Breast Cancer After Surgery

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Abstract. *Recurrent breast cancer (BC) tends to show an aggressive behavior and the number of cases of long-term survival is limited. Two rare cases of recurrent breast cancer were treated with a multidisciplinary approach. The outcome of the two cases indicated an excellent survival period of more than 13 years after recurrence. These findings suggest that patients who experience a recurrence after tumor resection have a chance of achieving long-term survival when treated with aggressive therapy, even in the presence of extensive metastases involving multiple organs.*

Breast cancer (BC) is a major cause of cancer-related death in females (1) and recurrent BC is lethal in most patients, despite many advances in treatment (2). In general, the first-line therapies are endocrine therapy for patients with estrogen or progesterone receptor-positive cancer and chemotherapy for patients with receptor-negative cancer (3, 4). The treatment of BC patients with metastases after failure of second-line treatment remains controversial because no drug has emerged as a gold standard. Moreover, the number of trials addressing the issue of salvage therapy as more than third-line management remains low (5). Therefore, it is difficult for clinicians to choose the optimal combination of surgery, radiation, and systemic therapy and there are few reports of long-term survival, especially for patients with metastasis to a single organ (6) and metastatic BC (7). Furthermore, there might be large differences between the type of chemotherapy for patients with advanced disease with a large tumor burden that could not be resected and patients with recurrence who had macroscopically tumor-free periods following complete resection.

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This report presents two successful cases of BC patients who received multidisciplinary treatment and who demonstrated an extended survival period of more than ten years after recurrence. The implications of these findings are also discussed and this information is presented to help determine the optimal treatment strategies for such patients.

Cases Report

Case 1. A left breast tumor was found in a 35-year-old female by her primary doctor. Modified radical mastectomy was performed for the breast cancer in October 1991. Postoperative histopathology findings were compatible with invasive ductal carcinoma (IDC) of the breast. The disease was stage IIA (T1N1M0) (8). Immunohistochemical staining of the cancer cells was negative for both estradiol and progesterone receptors. CEF (cyclophosphamide, epirubicin and fluorouracil) was administered because left supraclavicular lymph node metastases were found during a follow-up visit in October 1994. She underwent a resection of a left chest wall metastasis and reconstruction with a split thickness skin graft and the greater pectoral muscle in November 1998. The fourth, fifth, sixth, and seventh ribs were resected and reconstructed by a myocutaneous flap using the rectus abdominis muscle due to a local recurrence in September 1999. Paclitaxel was administered for right malignant pleural effusion in October 1999. She received docetaxel for supraclavicular lymph node metastasis in July 2000. Irradiation was administered for left neck lymph nodes metastases in May 2001. Intrathoracic injection of cisplatin was administered for right malignant pleural effusion in July. Multiple lung metastases were detected in October 2001. Local recurrence of the left chest wall and mediastinal lymph nodes metastases were also detected in February 2002. Therefore, carboplatin plus paclitaxel was administered. Radiation was administered for metastases of the lumbar vertebra in July 2002, for sternal bone metastases in January 2004, and for right iliac bone metastases in June 2004. Capecitabine was introduced in August 2004. Radiation was administered for metastasis of the left pubic and upper arm

bone in February 2005. Immunohistochemical staining of the cancer cells of the left chest wall metastasis was negative for Her2 (1+). It was not possible to choose the drugs most likely to control the progression of BC at that time. Therefore, herceptin plus docetaxel was administered for palsy of the left vocal cord due to a metastatic lesion around the *nervus laryngeus recurrens*. Thoracic pericardiectomy was performed for malignant pericardial effusion in July 2005. Tracheotomy was performed for complete palsy of left the vocal cord in March 2006. Although previous specimens were negative for both estradiol and progesterone receptors, the patient thereafter received anastrozole after menopause. She died of renal failure due to invasion around the urinary duct by lymph node metastases in the pelvic space in June 2009. She had survived for more than 14 years after the initial recurrence.

Case 2. A 43-year-old female had a medical history of right breast cancer. She had IDC of the breast that was diagnosed as T2N1M0 stage IIB (8). Immunohistochemical staining of the cancer cells was negative for both estradiol and progesterone receptors. She had been treated three years earlier by a modified radical mastectomy at another hospital. She received fluorouracil and goserelin acetate as adjuvant therapy and then moved to the host hospital for further treatment. Radiation therapy was administered for metastasis to the skin, bones of the skull, lower cervical vertebrae and she thereafter received CMF (cyclophosphamide, methotrexate and fluorouracil) and leuporelin in October 1997, followed by leuporelin until October 1998. Left axillary lymph node swelling was found and a biopsy was obtained. The histopathological examination confirmed a metastasis from the IDC of the breast with the same characteristics as the original tumor cells and immunohistochemical staining of the cancer cells was positive for both estradiol and progesterone receptors. Therefore, tamoxifen citrate was administered in December 1998. Radiation was administered for metastases of the right supraclavicular lymph nodes and sternal bone in July 2001. CAF (cyclophosphamide, adriamycin and fluorouracil) was administered in August 2001. She received anastrozole in March 2002 after menopause. Retrospective immunohistochemical staining of the cancer cells of the previous left axillary lymph node was negative for Her2. Radiation was administered for metastases of the upper cervical vertebrae, right iliac, lumbar vertebra, hip, pubic, left temporal, and forehead bone from June 2005 to June 2006. Exemestane was administered for metastases of the occipital bone, lung, and intrapulmonary lymph nodes in September 2008. Radiation was administered for metastases of the lower lumbar spine in April 2009. Toremifene citrate was again administered in May 2009. Radiation was given for metastases of the right iliac bone in May 2009. A right lung

tumor was detected during a follow-up visit. A transbronchial lung biopsy revealed squamous cell carcinoma of the lung that was diagnosed as T1aN0M0 stage IA (9). Radiation therapy was administered for lung cancer. The patient is currently in good condition and is being followed-up at the outpatient clinic without further evidence of disease progression. She has survived for more than 13 years after the initial recurrence.

Discussion

Most BC recurrences occur in the first within five years after initial treatment (10). Previous studies have reported a young age (11), large tumors (12), multiple tumors (13), positive tumor margins (14), axillary lymph node involvement (12), and extranodal extension (12) to be risk factors for recurrence. Both of the cases reported here involved relatively young patients and axillary lymph node involvement, which was consistent with the previous reports. In general, the reason for a long late interval between primary treatment and the first recurrence is thought to be due to slow tumor growth rate, hormonal and immunological control, and maintaining the cancer cells in a dormant state (15). Therefore, the good prognosis of patients with very late recurrence is attributed to their favorable response to the selected treatment modalities (16). However, the interval until recurrence in the presented cases was three years in case 1 and 3.5 years in case 2. As a result, a good clinical outcome was not observed. Nevertheless, they did survive for long periods.

There are three important issues associated with extended survival for patients with recurrent BC. A good interpersonal relationship is absolutely imperative between patients and the attending doctor for the selection of the modality of therapy. Medical attendants might provide an ideal counselor and partner to patients over a long period of time because they sometimes look for ways to control BC more efficiently through a trial-and-error process. In fact, herceptin was administered in case 1 in spite of negative immunostaining of Her2 because there was minor expression of Her2 (17) and tumors have been observed to change the Her2 status of the metastatic lesion (18). The clinical response was judged to be stable disease after two courses of herceptin with minor shrinkage, even though the treatment was stopped due to adverse events including digestive symptoms. Aromatase inhibitor controlled the recurrence for more than three years without massive progression in spite of negative immunostaining of hormone receptor. Knowledge of ongoing research is needed because medical research is continually producing new treatments (3). Furthermore, there is a need for an increased awareness of the possibility of a second malignant neoplasm, as in case 2, during the long-term follow-up of breast cancer patients harboring carcinogenic potential (19).

Conclusion

Patients who experience a recurrence after tumor resection have a chance of achieving long-term survival with multidisciplinary treatment, even in the presence of extensive metastases that include multiple organs. Continued emphasis on improving survival, and decreasing recurrence are the goals of ongoing breast cancer research.

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