

Case Report

A Case of Brachial Lymph Node Recurrences after the Resection of Locally Advanced Breast Cancer

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Keywords

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Abstract

We present a case of two recurrences in the brachial lymph nodes after initial resection, which was performed for radical cure. A 66-year-old woman was diagnosed with left breast cancer T4bN3cM0 Stage IIIC and an immunohistochemistry assay showed estrogen receptor (ER) positivity (5%), progesterone-receptor (PgR) positivity (1%), human epidermal growth factor receptor-2 (HER2) positivity (3+), and low Ki-67 (15%). After four courses of adriamycin and cyclophosphamide, followed by four courses of trastuzumab plus docetaxel, the patient underwent left mastectomy and axillary dissection. Postoperatively, she was diagnosed with breast cancer ypT1cN0M0, and trastuzumab and anastrozole were started. Postoperative irradiation was performed. Three years and 5 months after the initial breast cancer surgery, she had left brachial lymph node recurrence. It was resected, and tamoxifen was administered postoperatively. One year and 9 months after, she had another left brachial lymph node recurrence, and it was resected. She received radiation therapy to her upper limb and started taking exemestane. After 1 year and 3 months since the second recurrence surgery, there has been no recurrence. Our case suggests that the replacement of regional lymph nodes with tumor cells may result in the reconstruction of lymph flow to the upper arm and the development of brachial lymph node metastasis. There are no reports of resection of the recurrent tumor in the brachial lymph node for curative treatment. Therefore, careful follow-up is important in the future.

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Introduction

Breast cancer patients with distant metastasis are not indicated for treatment aimed at curing the disease, but are generally treated to prolong survival and maintain or improve quality of life [1]. Among them, some patients with limited metastatic burden will be treated with the intention of curing the disease. Metastasis to extra-regional lymph nodes is defined as a distant metastasis. However, when there is no distant metastasis to other organs, it is controversial whether or not surgery for curative purposes is possible. Contralateral axillary lymph node metastasis is classified as Stage IV, but it has been reported that curative treatment should be prioritized over palliative treatment because it can be considered a local recurrence in the absence of other distant metastases [2]. In addition, in patients with oligometastatic breast cancer, there have been some reports that local treatment can be performed on the metastatic lesions with a favorable clinical course [3–6]. We present a case of breast cancer recurrence to brachial lymph nodes wherein recurrence in the lymph node occurred twice after resection. We resected the brachial lymph node metastasis after initial surgery for breast cancer with the aim of providing a radical cure.

Case Presentation

A 66-year-old woman had no medical history or family history of cancer. She had been aware of her left breast mass for 6 months and went to the hospital because it had grown larger. A 4.5-cm mass was palpated in the upper outer quadrant of the left breast, and redness with skin edema was observed. Computed tomography (CT) showed a 4-cm mass in the upper outer quadrant of the left breast, enlarged lymph nodes in the internal mammary, axilla, supraclavicle, and subclavian regions, and there was no evidence of distant metastasis to other organs (online suppl. Fig. S1a, b; for all online suppl. material, see www.karger.com/doi/10.1159/000525295). Core needle biopsy was then performed, following which histopathology indicated invasive ductal carcinoma, histological grade 3, and an immunohistochemistry assay showed estrogen receptor (ER) positivity (5%), progesterone-receptor (PgR) positivity (1%), human epidermal growth factor receptor-2 (HER2) positivity (3+), and low Ki-67 (15%). She was finally diagnosed with left breast cancer T4bN3cM0 Stage IIIC. Preoperative chemotherapy was administered, including four courses of adriamycin and cyclophosphamide, followed by four courses of trastuzumab plus docetaxel, which resulted in a partial clinical response. Subsequently, she underwent left mastectomy and axillary dissection. Histopathology analysis of the surgically resected specimen of the breast showed invasive ductal carcinoma. The invasion depth was 1.4 cm, with no lymph node metastasis. Biomarker analysis using immunohistochemistry showed ER positivity (30%), PgR negativity, HER2 positivity (3+), and low Ki-67 (10%). She was finally diagnosed with ypT1cN0M0 breast cancer. Postoperative adjuvant therapy with trastuzumab (1 year) and hormonal therapy with anastrozole were started. Postoperative irradiation was performed on the chest wall, supraclavicular lymph nodes, and internal mammary lymph nodes (50 Gy in 25 fractions). At 3 years and 5 months after her initial surgery, she noticed a mass on her left upper arm during continuous anastrozole medication. A dynamic contrast-enhanced magnetic resonance imaging (MRI) scan revealed high signal intensity at T1-weighted imaging in the area of the left upper arm outside the muscles (Fig. 1a, b). Lymph node metastasis was suspected. Fine needle aspiration cytology was performed, which revealed a diagnosis of adenocarcinoma. We suspected lymph node recurrence of the left upper arm and performed resection for definitive diagnosis and treatment. The pathological results were ductal carcinoma, ER negativity (<1%), PgR positivity (<10%), HER2 positivity (3+), and high Ki-67 (30%), which were



Fig. 1. Dynamic contrast-enhanced MRI scan in T1-weighted fast field echo imaging. High signal intensity was found in a part outside of the muscle of the upper left arm. The image was taken in the coronal view (a), and the image was taken in the axial view (b).

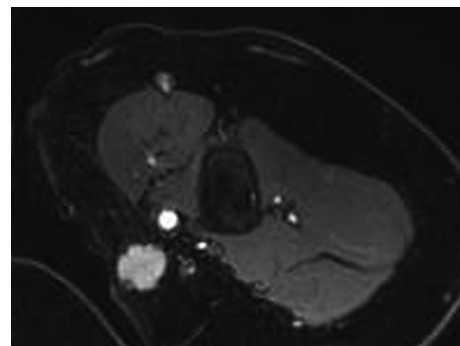
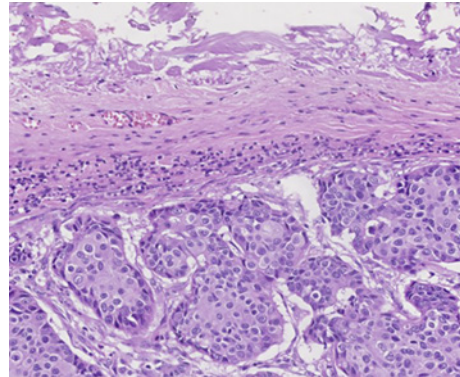


Fig. 2. Dynamic contrast-enhanced MRI scan in T1-weighted fast field echo imaging. The axial image shows high signal intensity at the same site as the previous brachial lymph node recurrence site.

consistent with the results of the initial breast cancer lymph node metastases. We suggested chemotherapy and radiation therapy as distant metastatic recurrence treatments, but she rejected all of them and was followed up only with oral tamoxifen. At 1 year and 9 months after resection for the recurrence, we noticed a mass near the surgical scar on the upper left arm while she was taking tamoxifen. A dynamic contrast-enhanced MRI scan revealed high signal intensity at T1-weighted imaging in the medial aspect of the left upper arm (Fig. 2). We performed a CT scan for the chest, abdomen, and pelvis to exclude any recurrence and found no evidence of metastases to other organs. We performed core needle biopsy, and histopathology findings indicated carcinoma, while the immunohistochemistry assay showed ER negativity (<1%), PgR positivity (2–3%), HER2 positivity (3+), and high Ki-67 (40%). In the background of small lymphocytes, polygonal cells formed vesicles with a tubular structure in part and proliferated invasively, which was a finding consistent with lymph node metastasis of previously known breast cancer. Positron emission tomography-CT imaging showed accumulation in the upper left arm, but positron emission tomography-CT at the time of the first diagnosis of breast cancer did not show any such accumulation (online suppl. Fig. S2a, b). We performed resection of the second recurrent tumor in the left brachial lymph node. Postoperative pathological results indicated ductal carcinoma, ER negativity, PgR negativity, HER2 positivity (3+), high Ki-67 (30%), and polygonal cells formed follicles against the background of small lymphocytes (Fig. 3). It was invasively proliferating, and we made a diagnosis of lymph node metastasis of breast cancer. After a

Fig. 3. Microscopic appearance of the surgical specimen (magnification $\times 200$). H&E staining allows the structure of a lymph node to be recognized, as lymphocytes are gathered in and around the fibrous capsule. In the lymph node, polygonal cells with enlarged nuclei and pale acidocyttoplasm form solid follicles, and proliferation of the cells can be identified. H&E, hematoxylin-eosin.



thorough discussion regarding postoperative treatment, the patient strongly requested not to receive chemotherapy. She received radiation therapy to her upper limb (50 Gy in 25 fractions) and started taking exemestane. It has been 1 year and 3 months since the second recurrence surgery, and there has been no recurrence.

Discussion

We encountered a case of two recurrences to the brachial lymph node after initial breast cancer surgery, a rare condition. No other similar case of brachial lymph node recurrence, clearly away from the axilla, has been found in our literature search. We hypothesized that the mechanism by which brachial lymph node metastasis occurred was as follows. The lymphatic channels of the breast are in the axillary direction, the lateral mammary gland direction, the sternoclavicular joint direction, and the internal mammary direction [7]. In our case, the axillary, supraclavicular, subclavicular, and internal mammary lymph nodes were filled with tumor cells when we performed the first breast cancer surgery. It is possible that the humeral lymph flow was reconstructed and metastasized accordingly to the brachial lymph node. Micro-metastasis in the brachial lymph node that originally existed at the time of initial breast cancer surgery may have developed because the upper arm was not irradiated by the post-mastectomy radiation therapy, while the supraclavicular and internal mammary lymph node areas were irradiated. This hypothesis is based on the anatomical regeneration of lymphatic flow patterns. In this case, the patient had breast cancer with weak hormone sensitivity but was positive for hormone receptors; therefore, endocrine therapy was administered as adjuvant therapy. However, the biology of the recurrent tumor showed that hormone receptors tended to become negative, and a hormone-insensitive tumor appeared. In particular, the brachial lymph node was more like a regional lymph node than a distant metastasis, and hormone therapy may not have contributed to local control. In contrast, two brachial lymph node metastases appeared, but she had breast cancer without distant metastasis to other organs, suggesting that chemotherapy, including anti-HER2 drugs, may have been effective systemically. The most recent edition of the American Joint Committee on Cancer (AJCC) Staging Manual, the eighth edition, defines ipsilateral axillary lymph nodes I-III, ipsilateral supraclavicular lymph nodes, and ipsilateral internal mammary lymph nodes as regional lymph nodes. Lymph node metastases other than local lymph nodes, such as the contralateral intramammary lymph node and the contralateral axillary lymph node, are considered distant metastases [8]. Maintenance or palliative treatment is usually the choice for Stage IV patients when metastases are found in extra-regional lymph nodes or distant

organs [9]. The brachial lymph nodes are extra-regional lymph nodes. Patients with brachial lymph node metastasis are not usually the targets of curative treatment, but this approach is controversial in the absence of metastases to distant organs. Metastatic breast cancer is relatively common, with 20–30% of patients with early-stage breast cancer developing metastases and with 3–6% of patients with breast cancer diagnosed as de novo stage IV [6]. Metastatic breast cancer is considered an incurable disease with poor prognosis, and surgery is considered to be palliatively performed only to relieve complications such as bleeding, pain, and infection [10]. However, patients with metastatic breast cancer are considered to be a very heterogeneous group, as 1–10% of these patients respond to treatment very well and have prolonged survival [4]. Lymph node metastasis of the contralateral axilla is referred to as a distant metastasis. However, Chkheidze et al. [2] argued that contralateral axillary lymph node metastasis is not hematogenous and is considered to be a regional spread of the tumor through the lymphatic vessels and should not be classified as distant metastasis. There are reports of good prognoses for breast cancer that shows metastasis to extra-regional lymph nodes. Oligometastatic disease means that only a few metastases can be found on systemic imaging, but there is no strict definition. A generally accepted definition of oligometastasis is no more than five metastases confined to a single organ. Some studies have defined oligometastasis as less than five metastases and smaller than 5 cm in size [11, 12]. It has been suggested that oligometastases exist in a transitional state between localized systemic disease and widespread systemic disease. Therefore, if the primary site is controlled or resected and the metastatic site is also resected, then the disease-free period will be extended, and perhaps the patient may be completely cured [13]. Kobayashi et al. [14] reported that 75 patients with oligometastatic breast cancer received systemic treatment, followed by local therapy, and had a 20-year overall survival rate of 52%. The analysis indicated that patients with oligometastatic breast cancer have long-term prognosis superior to those with other distant metastatic breast cancers. Survival data for surgical resection of oligometastatic breast cancer are primarily based on retrospective data analyses of multiple cases conducted in a single center or in multiple centers [6]. In oligometastatic breast cancer, surgery for metastases is still experimental because there are no data from prospective randomized trials with large samples [15]. Therefore, the efficacy and indications for the resection of metastatic sites remain controversial.

In conclusion, in our case, we performed surgery as a curative treatment because the tumor metastasized only to the brachial lymph nodes and was considered to have metastasized from the lymphatic tract. The possibility of a good prognosis was considered as a case of resection for oligometastasis. Since there are no reports of recurrence in the brachial lymph node resected for the purpose of radical cure, careful follow-up is important for case accumulation in the future.

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Statement of Ethics

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. This study protocol was reviewed, and the need for approval was waived by the Ethics Review Board of National Cancer Center Hospital East.

Conflict of Interest Statement

Tsuguo Iwatani received lecture fees from Eli Lilly, Asahi Kasei Medical, Novartis, and Pfizer. All remaining authors have no conflicts of interest to declare.

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Author Contributions

Kayono Onishi, Rurina Watanuki, Takamichi Yokoe, Tsuguo Iwatani, Chisako Yamauchi, and Tatsuya Onishi made significant contributions to the conception of this case report. Takamichi Yokoe contributed to facilitating the acquisition of the patient details. Kayono Onishi wrote the manuscript with important intellectual input from Rurina Watanuki, who also revised the draft critically. Rurina Watanuki, Takamichi Yokoe, Tsuguo Iwatani, Chisako Yamauchi, and Tatsuya Onishi have approved the final draft.

Data Availability Statement

All data that support the findings of this study are included in this article. Further inquiries can be directed to the corresponding author.

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