

Case Report

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# Pitfall in the Surgical Management of a Shrunken Skin Defect after Neoadjuvant Chemotherapy for Locally Advanced Breast Cancer

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## Keywords

Breast cancer · Locally advanced breast cancer · Neoadjuvant chemotherapy · Skin defect

## Abstract

A 53-year-old woman with a large, easy-bleeding, and ulcerated breast tumor visited our hospital due to severe anemia. Transfusion and Mohs' chemosurgery gave the patient marked improvement of her local and general condition. After confirming the human epidermal growth factor receptor type 2 (HER2)-positive breast cancer with no distant metastasis, anti-HER2 agents-containing chemotherapy brought about clinical complete response of the locally advanced breast cancer with a shrunken but still large skin defect. We, therefore, treated the patient with mastectomy and axillary node dissection but failed to directly close the skin even after full skin undermining. We then tried to cover the skin defect using a latissimus dorsi flap, that is, horizontal spindle skin 12 × 6 cm in size, but again failed to fully cover the skin defect. We finally and ostensibly covered the skin defect through an additional skin incision to the recipient skin, but could not get complete wound healing. Pathological study showed a marked collagen fiber around the skin defect and faint viable cancer cells beneath the nipple. The patient required 3 months of wound management for complete wound healing, leading to the application of anti-HER2 agents without anticancer agent to the patient during that time as an adjuvant therapy. Regrowth of her hair once lost by the neoadjuvant chemotherapy (NAC) made the patient refuse the adjuvant anthracycline-containing chemotherapy after wound healing. The patient, therefore, received trastuzumab-emtansine for a year and has been well for 17 months postoperatively. Breast surgeons should note that a skin defect after favorable response to NAC is often surrounded by less stretchable skin due to chemotherapy-induced massive collagen fiber and requires careful preoperative planning for skin closure.

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## Introduction

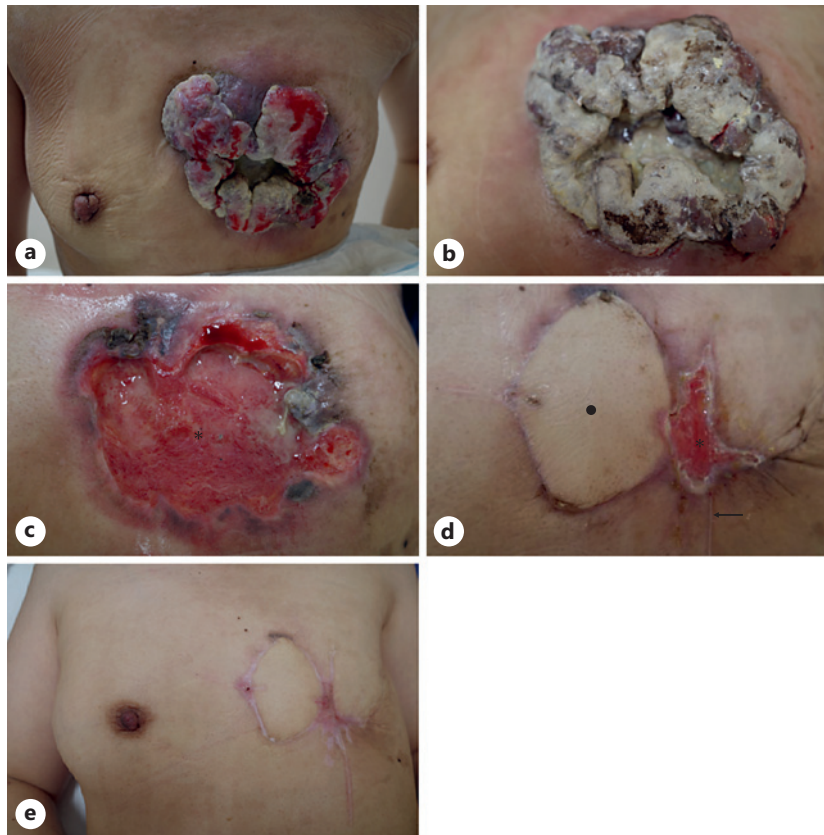
Human epidermal growth factor receptor type 2 (HER2)-positive subtype is an aggressive phenotype of breast cancer. In the 20th century, breast oncologists often struggled with how to treat HER2-positive locally advanced or metastatic breast cancer. The advent of various anti-HER2 agents such as trastuzumab, pertuzumab, trastuzumab-emtansine, and trastuzumab-deruxtecan has markedly changed the therapeutic strategy of HER2-positive locally advanced or metastatic breast cancer [1–3].

Even breast cancers larger than 5 cm can frequently show not only clinical complete response but also pathological complete response to anti-HER2 agent(s)-containing chemotherapy [4]. Therefore, many patients with a large HER2-positive breast cancer are often treated not only with mastectomy but also with breast-conserving therapy when the breast cancer shows favorable response to neoadjuvant chemotherapy (NAC). In the near future, in cases with clinical complete response to NAC, no surgical intervention to the breast should become an important therapeutic option when the anti-HER2 agent(s)-containing chemotherapy induces pathological complete response in the rebiopsy specimen after NAC.

Some locally advanced breast cancers lack normal skin due to direct invasion of breast cancer to the overlying skin, often showing unpleasant bleeding and discharge from the tumor. Complete or quasi-complete response to NAC annoys breast surgeons how to operate the regressed or disappeared breast cancers when the large skin defect still remains in the center of the lesion. We herein report a case of locally advanced and ulcerated HER2-positive breast cancer having shown a marked response to NAC but having required long-term postoperative wound management by insufficient skin covering due to poor preoperative surgical planning.

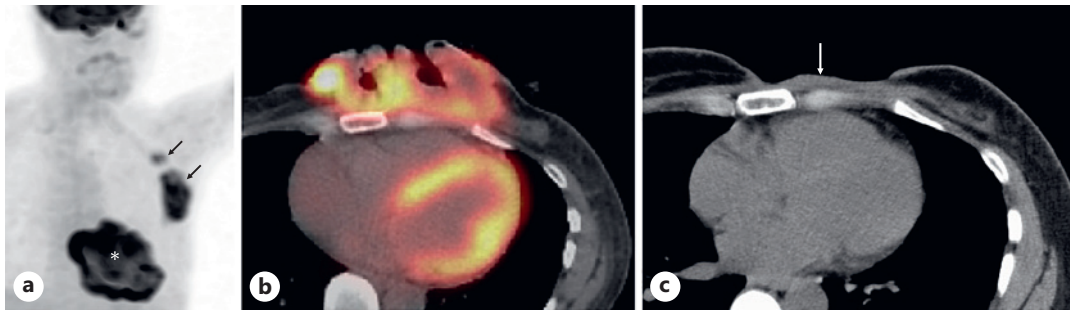
## Case Report

A 53-year-old woman with a large, easy-bleeding, and ulcerated breast tumor (Fig. 1a) visited our hospital due to anemia-induced dizziness. She had noticed her breast mass for 3 years. She had severe anemia, that is, serum hemoglobin level of 4.8 mg/dL, due to the repeated bleeding from the tumor. After the recovery from severe anemia by transfusion, we applied Mohs' chemosurgery [5] to the large tumor to control the bleeding, leading to the prompt hemostasis and successful blockade of massive exudation from the tumor (Fig. 1b). Core needle biopsy to the tumor, done before Mohs' chemosurgery, showed estrogen receptor-negative, progesterone receptor-negative, and HER2-positive atypical cells growing in solid and trabecular pattern. Positron emission tomography/computed tomography showed a large breast cancer and ipsilateral axillary lymph node metastases without distant metastasis (Fig. 2). Under the diagnosis of HER2-positive locally advanced breast cancer, the patient received combination chemotherapy using trastuzumab, pertuzumab, and docetaxel, leading to nearly complete regression both of the tumor (Fig. 1c, 2) and the enlarged axillary lymph nodes. We, therefore, did mastectomy to the left breast and dissected the axillary lymph nodes. Two of the dissected lymph nodes showed massive collagen fiber and no viable cancer cells. The resected breast showed an ulcerated lesion with massive collagen fiber, cholesterol crystals, and aggregation of foamy cells, showing only faint viable cancer cells just beneath the nipple (Fig. 3). Despite the presence of a shrunken but still relatively large skin defect even after NAC, we initially planned to directly close the skin simply with minimal skin safety margins and full skin undermining. Impossible direct skin closure, however, made us try to cover the skin defect by a latissimus dorsi musculocutaneous (LD-MC) flap grafting using

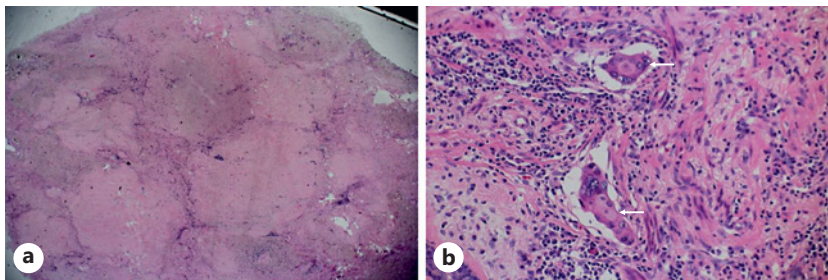


**Fig. 1.** Local findings. **a** A large, easy-bleeding, and ulcerated tumor was observed on the left chest wall. **b** Mohs' chemosurgery promptly stopped the bleeding from the tumor. **c** Almost complete tumor regression was observed after primary chemotherapy with a shrunken but still large skin defect (asterisk). **d** Even after the latissimus dorsi musculocutaneous flap grafting and further skin mobilization through skin incision to the recipient site skin, a skin defect (asterisk) was observed just lateral and cranial to the skin island (closed circle) and skin incisional line (arrow), respectively. **e** Three months' wound management brought about complete wound healing.

horizontal spindle-shaped skin  $12 \times 6$  cm in size. Based on the idea that it would be possible to easily fill the skin defect through a small skin transfer, we created the LD-MC flap using a spindle skin  $12 \times 6$  cm in size, that is, our usual manner, but failed to completely cover the skin defect. We, therefore, further tried to cover the skin defect with a skin mobilization through incising the recipient site skin. With this procedure and the addition of tensile sutures, the wound could be closed temporarily at least seemingly. Except for wound healing, the patient recovered uneventfully and was discharged on the 12th day after operation. A small skin defect, however, appeared just after suture removals on the outpatient basis. The patient needed approximately 3 months of wound management for the complete wound healing, that is, epithelization of the skin defect after LD-MC flap grafting (Fig. 1d,e), during which time the patient began to receive adjuvant trastuzumab and pertuzumab therapy, that is, no harm to the wound healing. After the complete wound healing, we proposed the patient to receive adjuvant anthracycline-containing chemotherapy. The patient, however, strongly requested us to receive some adjuvant therapy without the side effect of alopecia because the patient had already recovered from chemotherapy-induced hair loss. The patient, therefore, received trastuzumab-emtansine for 12 months as an adjuvant chemotherapy and has been well without any events for 17 months after operation.



**Fig. 2.** Images before and after neoadjuvant chemotherapy. **a** Positron emission tomography (PET) just after Mohs' chemosurgery showed marked uptake of fluorodeoxyglucose both in the tumor (asterisk) and ipsilateral axillar lymph nodes (arrows). **b** PET/computed tomography showed an ulcer-forming large tumor. **c** A large persistent skin defect (arrow) was still observed before operation.



**Fig. 3.** Pathological findings. **a** Massive collagen fiber predominated throughout the resected specimen. **b** Faint viable cancer cells (arrows) were observed just beneath the nipple.

## Discussion

In the past, the main purpose of NAC was, due to its tumor shrinkage effect, to enable surgery in inoperable cases and to enable breast conservation in cases for which breast-conserving surgery was not indicated. However, due to the advent of various effective new anticancer agents such as anti-HER2 agents, antiangiogenic agents, and immune check point inhibitors [6], even small breast cancers, that is, good candidates for breast-conserving therapy, have often come to be treated with NAC especially when the breast cancers are aggressive phenotypes such as triple-negative and HER2-type breast cancers. This trend is strongly based on the idea that pathological complete response after NAC, when proven after surgery, is a good predictive factor and nonpathological complete response cases can be further treated with additive adjuvant therapy for better clinical outcome [7].

Skin grafting and MC flap grafting are the two major methods to fulfill the skin defect in breast cancer surgery. In this case, we could have selected skin grafting, but actually we used LD-MC flap grafting to avoid possible surgical site infection due to the long-lasting skin defect. Of the three main MC-flaps often used in breast cancer surgery such as deep inferior epigastric perforator flap [8], transverse rectus abdominis MC flap [9], and LD-MC flap [10], the last one is best suited for skin covering in this case due to both its less invasiveness and stable blood flow compared with those of the other two flaps.

NAC brought about marked tumor regression and moderate shrinkage of the skin defect in this case. We thought that direct skin closure might be possible by making minimal skin safety margins and full skin undermining because final skin defect area after mastectomy in

this case was expected to be similar to those of primary mastectomy with standard skin safety margins. Skin defect, however, was much larger than we had expected before surgery after having made circumferential minimal skin resection just around the skin defect and additive skin incision toward the axilla for lymph node dissection, having led to apparently impossible direct skin closure. We, therefore, tried to cover the skin defect by the LD-MC flap using horizontal spindle skin 12 × 6 cm in size, that is, our routine manner. This inevitable but careless LD-MC flap creation further led us to the insufficient covering of the skin defect.

Skin width of the LD-MC flap is naturally limited by the tension on skin closure at the donor site. But, if we had been more cautious about appropriate LD-MC flap creation, skin length should have been made much longer, that is, larger than 12 cm, for the skin covering in this case. In addition, some LD-MC flaps with nonround skin island fail to cover the skin defect due to the mismatch of long axis even when area of the flap skin is close to that of skin defect. The patient did not complain anything for the postoperative outcome because we had obtained full informed consent about the surgical adverse events including total flap loss. We, however, should have carefully decided the angle and length of the skin island to appropriately cover the skin defect.

Breast surgeons often make enough skin undermining for better cosmetic outcome in breast-conserving surgery and for safer skin closure in total mastectomy. Feasibility of this procedure strongly depends on the skin stretchability. Pathological findings of the resected specimen well explain the reduced stretchability of the skin caused by NAC-induced massive fibrosis. Breast surgeons should note this reduced stretchability of the skin at the recipient site when designing the size and angle of skin island for LD-MC flap after favorable response to NAC.

In conclusion, breast surgical oncologists should note the less stretchability of the skin around the skin defect after NAC to avoid insufficient skin covering with LD-MC flap and carefully plan how to cover the skin defect when present after NAC. The CARE Checklist has been completed by the authors for this case report, attached as the supplementary material.

### Statement of Ethics

The study was approved by the Kishiwada Tokushukai Hospital Ethics Committee (IRB #Case 22-7). Written informed consent was obtained from the patient for the publication of this case report and any accompanying images.

### Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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### Author Contributions

Hitomi Matsuki contributed to the design of the report. Shoji Oura drafted the manuscript. Shinichiro Makimoto revised the manuscript.

### Data Availability Statement

All data generated during this study are included in this article. Further inquiries can be directed to the corresponding author.

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