

Case Report



Successful Pre-Operative Local Control of Skin Invasion of Breast Cancer Using a Combination of Systemic Chemotherapy and Mohs Paste

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ABSTRACT

Locally advanced breast cancer (tumor > 5 cm, widespread infiltration of the skin and muscle, or metastases to lymph nodes) is difficult to resect by surgery, and even when it is resectable, there is a high probability of local recurrence and distant metastasis. Therefore, systemic therapy should be administered first. However, as cutaneous infiltration progresses, the patient's quality of life is impaired by pain, bleeding, presence of exudates, and a foul-smelling odor. Treatment with Mohs paste with systemic therapy can control symptoms associated with skin infiltration and can also be expected to decrease tumor volume. Herein, we report a case in which a tumor was resected following Mohs paste and systemic chemotherapy administration, and the skin defect was reconstructed with a latissimus dorsi myocutaneous flap. We also review the literature for previously reported cases of breast cancer involving Mohs paste.

Keywords: Breast neoplasms; Drug therapy; General surgery; Myocutaneous flap; Zinc

INTRODUCTION

Locally advanced breast cancer with cutaneous infiltration can significantly impair a patient's quality of life (QOL) due to pain, bleeding, presence of exudates and a foul-smelling odor. Patients with breast cancer have the highest prevalence of malignant wounds (47.1%) [1]. Such cases are often difficult to manage, and this condition can cause not only a decrease in the QOL due to a reduced motivation to engage in activities but also a decrease in motivation to continue treatment. Resection is performed as a symptomatic treatment if the general condition is good, but unfortunately, the risk of surgery is not associated with the survival rate. Radiation and chemotherapy may be effective, but it can take time for the effects to appear, and the symptoms may worsen due to disintegration. There have been reports of anti-cancer drug-containing ointments and antibacterial drug ointments, but their effects have not been established [2].

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Conflict of Interest

The authors declare that they have no competing interests.

Author Contributions

Conceptualization: Takeuchi M, Katsuki T, Iwamura M; Investigation: Takeuchi M, Katsuki T, Yoshida K, Onoda M, Iwamura M, Inokuchi T, Furutani A, Katoh T, Kawano K, Hirata K; Supervision: Katoh T, Hirata K; Validation: Takeuchi M; Visualization: Takeuchi M; Writing - original draft: Takeuchi M, Katsuki T; Writing - review & editing: Katsuki T, Iwamura M, Hirata K.

Mohs paste is a tissue fixative containing zinc chloride as the main component and is used in chemosurgery for malignant tumors of the skin [3]. It has been reported to be useful for improving symptoms and the QOL in patients with unresectable skin tumors, including metastasis [4-6]. Mohs paste has an immediate effect and is inexpensive. In addition, pain associated with chemical fixation can be controlled by the oral administration of non-steroidal anti-inflammatory drugs.

Recently, the use of Mohs chemosurgery has become widespread for the primary purpose of improving QOL. Mohs chemosurgery chemically fixes and removes lesions, such as skin cancer, and when performing a histopathological diagnosis of tissue samples, this procedure consists of a radical resection that repeats fixation, followed by the removal of the tumor until all traces of the tumor disappear on microscopic examinations. Compared to surgical resection, the procedure is simpler, less invasive, does not require special equipment, and can be performed even in cases where surgical resection is difficult [3,7].

Herein, we report a case of a locally advanced breast cancer in which the patient underwent radical surgery with reconstruction by a latissimus dorsi musculocutaneous flap after a combination of systemic therapy and Mohs paste and review currently published cases of Mohs paste being used to treat breast cancer patients along with a discussion of the clinical characteristics, treatment, and surgical indications to improve the QOL of breast cancer presenting with malignant wounds.

CASE REPORT

A 64-year-old woman visited our hospital complaining of a right breast mass with pain, bleeding and exudates and was foul-smelling. She had been aware of bleeding from the nipple for the past nine months. On admission, the mass was 13 cm in diameter, measured laterally from the nipple, and included the central portion of the breast. Skin infiltration and fixation of the chest wall were observed (**Figure 1A**). The hard axillary lymph nodes were palpable. Some tumor markers showed abnormal values, including carbohydrate antigen 15-3 (CA15-3; 1082 U/mL), NCC-ST-439 (33.0 U/mL) and BCA225 (1,442 U/mL).

Computed tomography (CT) revealed a tumor with a maximum diameter of 88 mm with an unclear border between the pectoralis major muscle and swollen lymph nodes in the right axilla (**Figure 1B**). However, no distant metastases were observed. A core needle biopsy was performed, and histopathologic examination revealed invasive ductal carcinoma-papillotubular carcinoma that was estrogen receptor-negative, progesterone receptor-negative, and human epidermal growth factor receptor 2-negative, with a Ki-67 index of 80%, suggesting triple-negative cancer. The patient was hospitalized, and fluorouracil (500 mg/m²) + epirubicin hydrochloride (100 mg/m²) + cyclophosphamide (500 mg/m²) (FEC) was selected as the first systemic therapy. After four cycles of FEC, it was changed to weekly paclitaxel (100 mg/m²), and she underwent systemic chemotherapy for a total of 10 months.

In parallel with the systemic therapy, written informed consent was obtained from the patient, and Mohs paste was applied to control local bleeding and exudates. Zinc chloride was pulverized into a powder and dissolved in purified water, and zinc oxide starch powder was gradually mixed. Finally, glycerin was added to achieve a viscosity that was individualized to the patient's needs (**Table 1**). After petroleum jelly was applied to the surrounding normal

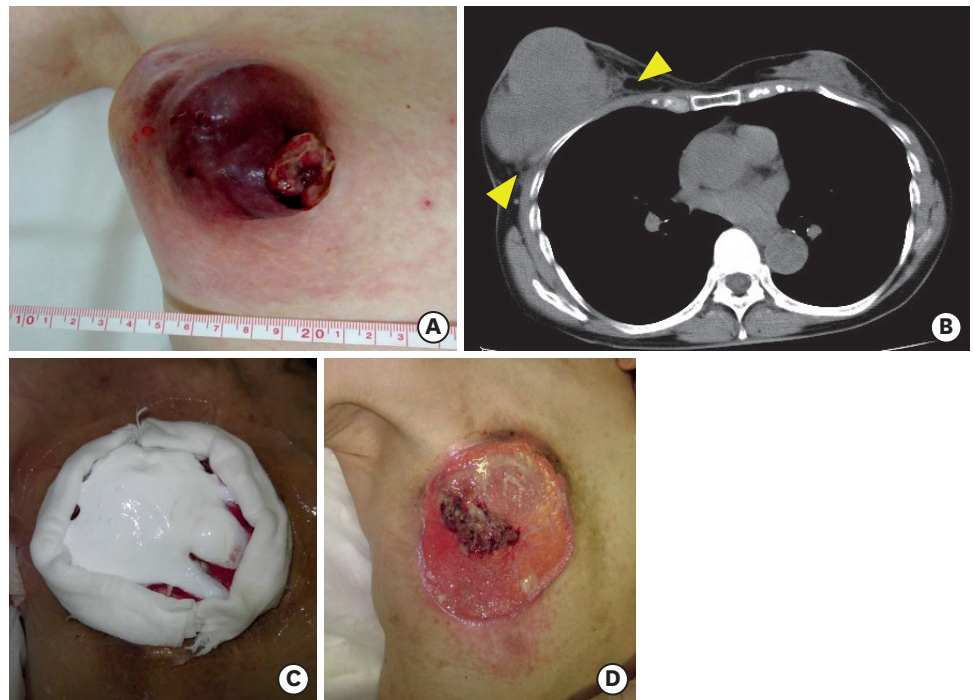


Figure 1. Macroscopic and CT image of the right breast at the initial visit and Mohs chemosurgery. (A) The tumor was approximately 13 cm with cutaneous infiltration mainly in area C of the right breast. Mobility was poor, and axillary lymph nodes were swollen. (B) CT revealed a mass with infiltration of the pectoralis major muscle (yellow arrowhead). (C) First, petroleum jelly was applied to the surrounding normal skin, and then Mohs paste was applied to the tumor and removed again after 24 h for observation of the tumor, with the cycle repeated as necessary. (D) Macroscopic image of the right breast before surgical treatment. The tumor was fixed by the effect of the Mohs paste, and necrotic tissue was removed bluntly. The process of applying paste, performing observation, and sacrificing necrotic tissue was repeated for 10 months. As a result, most of tumor was shaved off, until only a small amount remained in the center. CT, computed tomography.

Table 1. Formulation of Mohs' paste

Material	Original method [3,7]	Our hospital
Saturated zinc chloride	34.5 mL	
Zinc chloride		25 g
Purified water		15 mL
Powdered <i>Sanguinaria canadensis</i>	10 g	
Zinc oxide starch powder		30 g
Paste containing stibnite	40 g	
Glycerin		15 mL

skin, Mohs paste was applied to the tumor and then removed after 24 hours (**Figure 1C**). The tumor was observed daily, and the fixed tissue was gradually resected. After 10 months, the tumor nearly resembled a skin ulcer, and only a small amount of tumorous lesion remained in the center (**Figure 1D**). CT showed that the tumor volume had remarkably decreased, and the swollen lymph nodes in the right axilla had disappeared. Furthermore, all tumor marker values were within the normal limits.

The patient then underwent radical surgery with partial resection of the pectoralis major for the remaining tumor (**Figure 2A**), and the resulting large defect was reconstructed using a latissimus dorsi musculocutaneous flap (**Figure 2B**). In brief, the incision of the flap was extended laterally from the defect, and the latissimus dorsi was mobilized and passed under the axilla. The defect and flap were then sutured (**Figure 2C**). The engraftment of

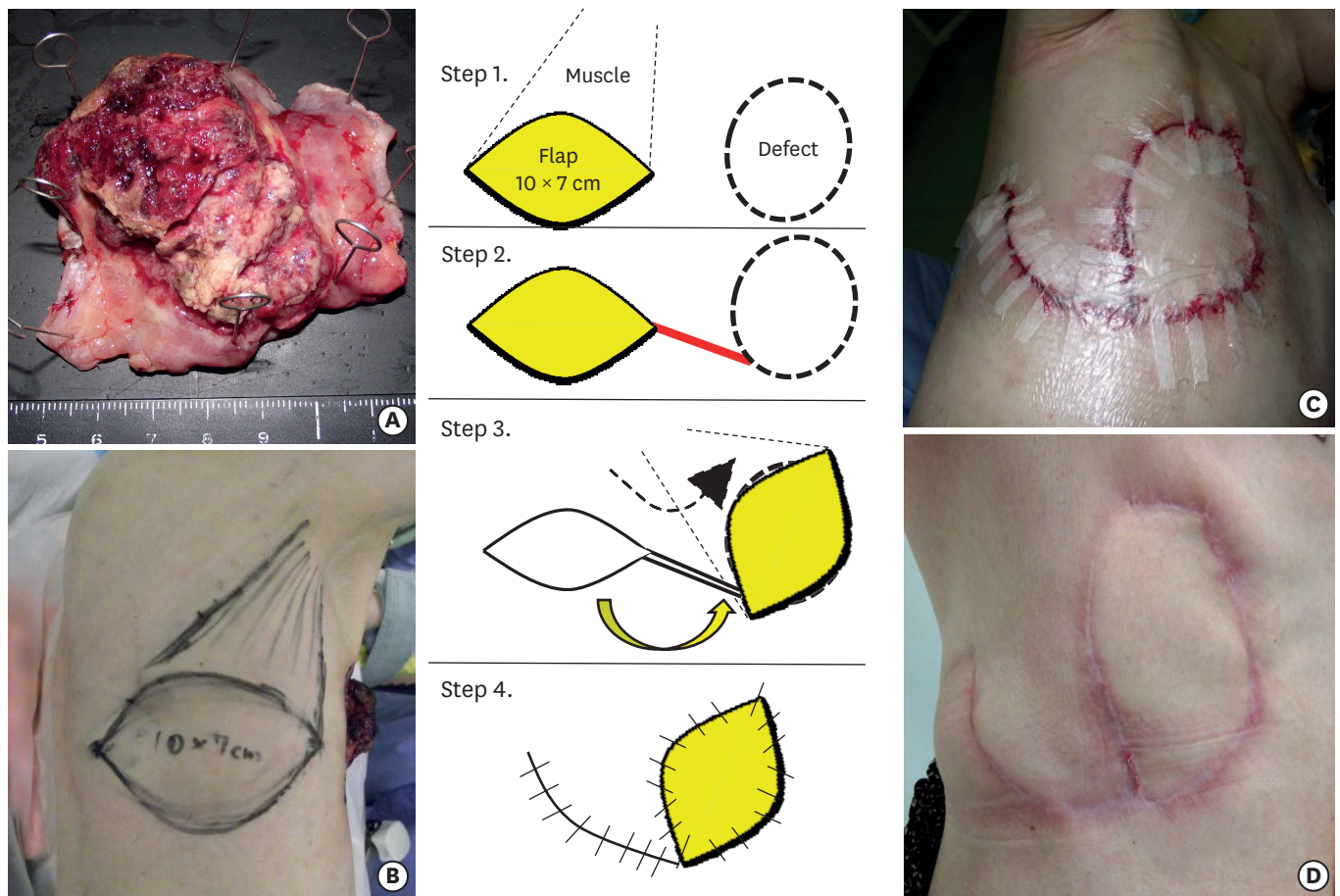


Figure 2. Radical surgery and reconstruction by latissimus dorsi musculocutaneous flap. (A) Resected specimens. The remaining tumor was resected along with a part of the pectoralis major. (B) The flap was designed in a spindle form (10 × 7 cm) that could cover a defect of the right chest (Step 1). To mobilize the flap, an incision was made between the flap and defect and was connected (Step 2). The latissimus dorsi musculocutaneous flap passed under the axilla and filled in the defect (Step 3). Finally, the flap was sutured (Step 4). (C) State at the end of surgery. (D) No engraftment failure was observed, and no recurrence or metastasis of the breast cancer has been observed for 10 years.

the musculocutaneous flap was good, and no obvious recurrence or distant metastasis was observed 10 years after the operation (**Figure 2D**).

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

DISCUSSION

Recently, in addition to reports in the field of palliative care on ways to improve the QOL by controlling bleeding and malodor, there have been many reports from Japan on the utility of Mohs paste for the initial treatment of locally advanced breast cancer. A search of PubMed and Ichushi-web was performed to identify the relevant case reports and case series using the following terms: “breast cancer” and “Mohs paste.” We identified 39 articles published between 2008 and 2020 in Japan, of which 59 included complete information. Of all the included cases, 36 involved the use of Mohs paste for a primary lesion. A summary of this systematic review is presented in **Table 2** [8-37].

Efficacy of Mohs Chemosurgery toward Breast Cancer Presenting Malignant Wound

Table 2. Summary of data in 37 cases of breast cancer and Mohs paste reported in the literature

Case	Age (yr)/sex	Symptoms	Pathology	ER/PgR/HER2	T	N	M	Stage	Chemo-therapy	Hormonal therapy	The day of improved symptoms (days)	Response	Salvage operation	Reconstruc-tion	Adverse events	Outcome	Ref
1	59/F	Bleeding, exudate, stink	Scirrhus, invasive ductal carcinoma	+/-/-	4d	1	1	IV	+	-	1	CR	-	-	Pain	Died 1.5 years later	8
2	47/F	Bleeding, exudate, stink, movable restriction of arm	Scirrhus, invasive ductal carcinoma	+/+/+	4b	2	1	IV	+	-	1	CR	+	Split skin graft	-	Improved	9
3	51/F	Bleeding, exudate, stink	X	X	4b	X	1	IV	+	X	60	PR	-	-	-	Improved	10
4	57/F	Bleeding, exudate, stink, respiratory discomfort	X	-/-/+	4b	2	1	IV	+	-	90	PR	-	-	-	Improved	11
5	40/F	Bleeding, exudate, stink	X	-/-/-	X	X	1	IV	-	X	1	PR	-	-	Pain, bleeding	Died 1 month later	12
6	52/F	Bleeding, exudate, stink	G-CSF producing, squamous cell carcinoma, Scirrhus, invasive ductal carcinoma	+/+/-	4b	3	1	IV	+	-	1	PR	-	-	Bleeding	Died 11 months later	13
7	55/F	Bleeding, exudate, stink	X	-/-/+	4b	3	1	IV	+	-	3	PR	-	-	-	Improved	14
8	60/F	Bleeding, exudate, stink	X	X	4c	X	1	IV	-	-	1	PR	-	-	Pain	NA	15
9	45/F	Bleeding, exudate	X	X	X	X	X	X	X	X	1	PR	X	X	-	Improved	16
10	70/F	Bleeding, exudate, stink	Scirrhus, invasive ductal carcinoma	+/+/-	4b	0	0	IIIB	+	-	1	CR	-	-	-	Died 4.5 years later	17
11	73/F	Bleeding	Invasive ductal carcinoma	+/+/-	4b	2	0	IIIB	-	+	30	PR	-	-	Pain, dermatitis	Improved	18
12	56/F	Bleeding	Scirrhus, invasive ductal carcinoma	+/+/-	4b	1	1	IV	-	+	90	PR	-	-	-	Improved	19
13	70/F	Bleeding, exudate, stink	Invasive ductal carcinoma	-/-/-	4b	1	0	IIIB	+	-	1	PR	+	Split skin graft	-	Improved	20
14	54/F	Bleeding, exudate	Invasive ductal carcinoma	-/-/+	4b	2	1	IV	+	-	6	PR	-	-	-	Improved	20
15	77/F	Bleeding, exudate	X	X	X	X	X	X	X	X	30	PR	-	-	-	NA	21
16	56/F	Bleeding, exudate	Invasive ductal carcinoma	+/+/+	4b	1	1	IV	-	+	3	PR	-	-	Pain	Improved	22
17	56/F	Bleeding, exudate, stink	X	+/-/+	4b	1	1	IV	-	+	NA	PR	-	-	-	Died 6 months later	23
18	58/F	Bleeding, respiratory discomfort	X	-/-/-	4b	1	0	IIIB	+	-	60	PR	+	Split skin graft	-	Improved	23
19	66/F	Bleeding, exudate, stink	X	X	4b	X	1	IV	+	-	30	PR	-	-	-	NA	24

(continued to the next page)

Efficacy of Mohs Chemosurgery toward Breast Cancer Presenting Malignant Wound

Table 2. (Continued) Summary of data in 37 cases of breast cancer and Mohs paste reported in the literature

Case	Age (yr)/sex	Symptoms	Pathology	ER/ PgR/ HER2	T	N	M	Stage	Chemo-therapy	Hormonal therapy	The day of improved symptoms (days)	Response	Salvage operation	Reconstruc-tion	Adverse events	Outcome	Ref
20	60/F	Bleeding	Papillotubular carcinoma	+ / + / +	4	3	1	IV	-	+	1	PR	-	-	Pain, dermatitis	Improved	25
21	35/F	Bleeding, exudate	X	+ / + / +	4	X	1	IV	+	+	14	PR	-	-	Pain, infection	NA	26
22	60/F	Bleeding, exudate, stink	Invasive ductal carcinoma	- / - / -	4c	1	1	IV	+	-	1	PR	-	-	-	Died 6 months later	27
23	50/F	Bleeding, exudate, stink	Invasive ductal carcinoma	+ / - / +	4c	0	1	IV	+	-	30	CR	-	-	Pain	Improved	28
24	104/F	Bleeding	X	- / -	4	1	0	IIIB	-	X	1	PR	-	-	-	Died 2 months later	29
25	68/F	Bleeding	X	+ / + / +	4c	1	0	IIIB	+	+	30	CR	+	Split skin graft	-	Improved	30
26	49/F	Bleeding	X	X	4b	X	1	IV	+	-	14	PR	+	-	-	Improved	31
27	64/F	Bleeding, exudate, stink	X	X	X	X	X	X	+	-	455	PR	-	-	-	Improved	31
28	55/F	Bleeding, exudate, stink	X	X	X	X	X	X	+	-	60	PR	+	X	X	Improved	31
29	90/F	Bleeding, exudate, stink	X	X	X	X	X	X	-	+	60	PR	-	-	-	Improved	31
30	81/F	Bleeding, exudate	Invasive lobular carcinoma	+ / + / -	4c	0	1	IV	-	+	60	CR	-	-	-	Improved	32
31	61/F	Bleeding, exudate, stink, respiratory discomfort	X	+ / + / -	4c	2	1	IV	+	+	1	PR	-	-	-	Improved	33
32	65/F	Bleeding, exudate	Invasive ductal carcinoma	+ / + / +	4c	0	0	IIIB	+	-	30	PR	-	-	-	Improved	34
33	68/F	Bleeding, exudate	Mucinous carcinoma	+ / + / -	4b	1	0	IIIB	+	+	2	PR	+	Split skin graft	Pain	Improved	35
34	66/F	Bleeding, exudate, stink	Invasive ductal carcinoma	- / - / -	4b	1	0	IIIB	+	-	1	PR	+	Split skin graft	-	Improved	36
35	50/F	Bleeding, exudate, stink	Scirrhus, invasive ductal carcinoma	+ / + / +	4	3	1	IV	-	+	10	CR	-	-	-	Died 9 months later	37
36	40/F	Bleeding, exudate	Scirrhus, invasive ductal carcinoma	- / - / -	4	2	1	IV	+	-	32	PR	-	-	-	Improved	37
Our case	64/F	Bleeding, exudate, stink	Papillotubular carcinoma	- / - / -	4b	1	0	IIIB	+	-	2	PR	+	Latissimus dorsi muscu-locutaneous flap	-	Improved	-

ER, estrogen receptor; PgR, progesterone receptor; HER2, epidermal growth factor receptor 2; T, tumor; N, node; M, metastasis; Ref, reference; CR, complete response; X, not appeared; PR, partial response; NA, not analyzed.

The average patient age at onset was 60.3 (range: 35–104) years, and stage IV disease was seen in 68.7% (22/32) of all cases. Interestingly, symptoms were controlled within 24 hours in 36.1% (13/36) of the patients. Furthermore, all cases showed a reduction in tumor volume (measured using RECIST version 1.1) [38]. Complete tumor removal was achieved in 25% (9/36) of patients. However, 96.9% of cases with complete information (31/32) were concurrently administered chemotherapy and/or hormonal therapy. Adverse events due to Mohs paste occurred in 27.8% (10/36), with complaints of “pain” in most cases. After

performing systemic chemotherapy and applying Mohs paste, 25% of cases underwent salvage surgery (9/36). Most patients underwent reconstruction with a split skin graft, and a pedicle graft, such as a latissimus dorsi musculocutaneous flap, was only used in our case.

Mohs paste, also known as Mohs chemosurgery, was developed by Frederic E. Mohs in the 1930s [3]. This method was originally applied for fixing and collecting histopathological tissue using the fixing and corrosive ability of zinc chloride, which is the main component. The underlying mechanism involves zinc ion precipitating proteins in an aqueous solution, which causes a tissue-astringent action and corrosion.

Mohs chemosurgery has primarily been used to treat patients with skin cancer, head and neck cancer, genital cancer and breast cancer [6,39-41].

Inoperable advanced breast cancer and locally recurrent lesions produce large amounts of exudate and necrotic tissue from the lesion. Such tissue can easily become infected by anaerobic bacteria, and thus give off a foul odor. In addition, these lesions easily bleed and become very difficult to manage, with episodes of bleeding in every dressing change. Such issues markedly impair a patient's QOL.

Mohs chemosurgery is less invasive than other approaches and does not require any special techniques or equipment. Most importantly, it can improve a patient's QOL and is expected to reduce tumor volume through gradual resection. Furthermore, management is easy and wound pain can be controlled by the administration of nonsteroidal anti-inflammatory drug. Such improvements can bolster the patients' motivation to continue therapy.

Mohs chemosurgery is not a first-line choice, but good results have been reported in cases of skin tumors [5,42]. Multidisciplinary treatment should be applied in locally advanced breast cancer [43]. In Japan, Mohs chemosurgery has frequently been reported for local control of advanced breast cancer or local recurrence, showing that Mohs chemosurgery can rapidly improve symptoms and facilitate tumor reduction when combined with multidisciplinary treatment.

The combination of systemic therapy and Mohs paste can be expected to markedly improve a patient's QOL and contribute to a good prognosis, and it may be the first choice for the treatment of advanced breast cancer.

From the perspective of curability, appearance and infection, resection of the primary lesion is often performed in cases that have shown some reduction by systemic therapy and Mohs paste. Many cases have undergone reconstruction with a split skin graft, although such cases presumably involve a small defect area due to tumor reduction and good granulation. A split skin graft has the benefit of being able to be collected flexibly, depending on the purpose and site of use, and is minimally invasive; however, it has the drawback of inducing skin contraction and notable pigmentation [44]. The present case had a large defect and poor granulation and needed a thick, wide area. While a latissimus dorsi musculocutaneous flap is more invasive than a split skin graft, it strongly connects muscle and skin and does not cause cosmetic issues [45]. Therefore, when planning reconstructive surgery, the strengths and weaknesses of the graft and flap should be carefully considered and the indications should be determined according to the size of the defect and the degree of the observed granulation.

We encountered a case of a locally advanced breast cancer with good results after systemic therapy, Mohs chemosurgery and radical surgery with reconstruction using a latissimus dorsi musculocutaneous flap.

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