Surgical Treatment Using Artificial Dermis for Women with Locally Advanced Breast Cancer

Tadahiro NOZOE[*1], Emiko NOZOE[*1] and Rie GONDO[*2]

*Department of [*1]Surgery and [*2]Plastic Surgery, Saiseikai Fukuoka General Hospital*

(Received June 13, 2022; Accepted July 26, 2022)

Physicians occasionally come across with patients with locally advanced breast cancer (LABC) bringing about distress, due to tumor growth, invasion to the skin, bleeding or an ill smell. Physicians often experience much difficulty in selecting and administering therapeutic option. The clinical courses of patient who had been treated with total resection of LABC and an attachment of artificial dermis (TERUDERMIS) were mentioned. Elimination of the symptoms derived from the tumors could be successfully accomplished for all of the patients. Except for one patients who initially had bone metastasis and died 13 months after operation, the other patients have been alive under preferable condition without any signs for tumor recurrence. The surgical resection and an attachment of artificial dermis is quite reliable and helpful for both patients and physicians in palliating symptoms and reducing care for infections and hemorrhage due to LABC.

Key words: locally advanced breast cancer, artificial dermis, quality of life

INTRODUCTION

Despite the ongoing national effort to detect breast cancer in the earliest stage, including mammography and ultrasonography screening [1, 2], we have occasionally been referred women with locally advanced breast cancer (LABC) that was discovered upon consultation with their physicians.

Patients with such significantly advanced tumors that have been left untreated, exhibit symptoms of chronic pain due to ulceration of the skin, hemorrhage due to large and deep wounds, and terrible drainage and ill smell due to tumor necrosis and/or infection.

Women with such advanced breast cancers, that had either been neglected or that were left unaware of, often present with such symptoms, and occasionally are enthusiastic for immediate alleviation of the distressing symptoms brought about by the tumors.

Due to the advanced stage of the disease limiting the patients' life, palliation, with reducing the time to recover and maintaining the quality of life, is essential. Moreover, the therapeutic option should also be as minimally invasive as possible.

In the current study, we examined the usefulness of reconstruction using attachment of an artificial dermis after total resection of LABC to contribute to improve the patients' quality of life.

PATIENTS AND METHODS

Enrolled patients

Three patients with LABC were referred to us. The clinical courses of these patients who had undergone treatment with total resection of the tumor and attachment of an artificial dermis were described.

This study was approved by the institutional ethics committee of Saiseikai Fukuoka General Hospital.

The clinical and pathologic features are shown in Table 1 and 2, respectively. All of the patients exhibited serious symptoms including pain, hemorrhage, and ill smelling infectious drainage.

Treatment

The tumor was dissected along with surrounding skin that was likely due to be cancer invasion. As the large tumors often contain so abundant feeding vessels, they were also carefully dissected. We aimed to spare the fascia of the pectoral muscle as much as possible (Fig. 1a–c, 2a–c, and 3a–c). The artificial dermis (TERUDERMIS) was then attached to fill up the defect of the skin (Fig. 1d, 2d, and 3d). When the wound healing was advanced with significant granuloma proliferation (Fig. 1e, 2e, and 3e), skin transplantation was performed using an autologous graft that was usually isolated from a femoral or abdominal portion (Fig. 1fg, 2f, and 3fg). Subsequently, a secondary treatment including axillary lymph node dissection and drug-induced therapy would be added.

RESULTS

The clinical views of the patients are shown in Fig. 1–3. The perioperative and postoperative courses of the patients are shown in Table 3. The operative period ranged between 54 and 95 minutes. Elimination of the symptoms derived from the tumors was successfully achieved for all patients. Moreover, we did not observe any postoperative complications. While two of the patients have since continued to be alive without any signs of tumor recurrence and with a generally satis-

Tadahiro NOZOE, Department of Surgery, Saiseikai Fukuoka General Hospital, 1-3-46, Tenjin Chuo Ward, Fukuoka 810-0001, Japan
Tel: +81-92-771-8151 Fax: +81-92-716-0185 E-mail: paper7777@yahoo.co.jp

Table 1 Clinical characteristics of the patients

Patients	Age	Chief symptoms	Initial metastasis
1	72	Hemorrhage	None
2	81	Hemorrhage, ill odor	None
3	75	Pain, ill odor	Bone

Table 2 Pathologic characteristics of the tumors

Patients	Maximum	Histology	ER/PgR/HER2	Ki-67	Nuclear grade
		Size (mm)		(%)	
1	100	NE	(+)/(+)/(-)	12	1
2	100	PT	(+)/(+)/(-)	28	1
3	130	PT	(-)/(-)/(-)	28	3

NE; neuroendocrine carcinoma, PT; papillotubular carcinoma

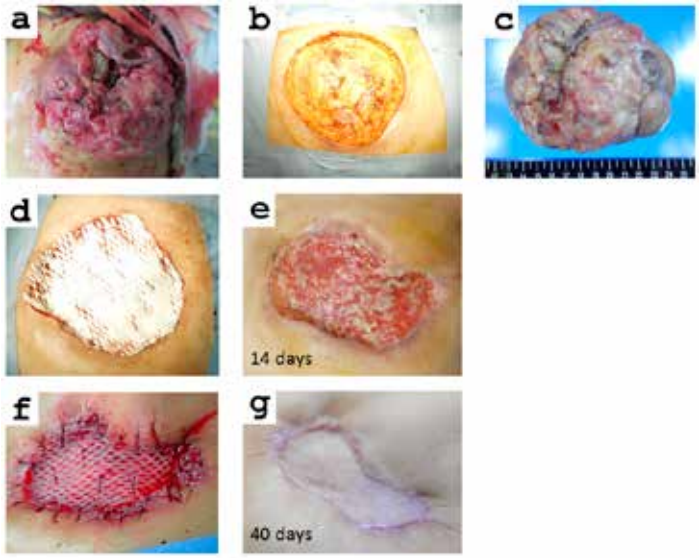

Fig. 1 Operative findings in Case. 1
a: A huge tumor measuring 10 cm was found on the left breast with hemorrhage and infected drainage.
b: Chest wall after dissection of the tumor.
c: Dissected tumor.
d: An artificial dermis (TERUDERMIS) was attached.
e: Wound 14 days after attachment of the artificial dermis, showing a favorable wound healing.
f: Skin transplantation using an autologous graft was performed.
g: Complete healing of the wound (40 days after skin transplantation).

factory condition, one patient died of recurrent tumors in the brain 21 months after the operation.

PRESENTATION OF A REPRESENTATIVE CASE

A 72-year old woman, who had a huge tumor on the left breast had been emergently transferred to our institute due to continuous bleeding from the tumor. While she had been aware of the gradual growth of the tumor, she avoided seeing a physician. As the tumor began to exhibit hemorrhage, pain and ill smelling drainage, spoiling her daily life, she eventually reached out to our institute. She confessed that she had wiped the ill smelling drainage using two boxes of tissue-paper per day, which might be quite unsanitary.

A huge tumor was found on the left breast with broad skin invasion bringing about hemorrhage and infected drainage (Fig. 1a).

In the laboratory examinations, and there was no increase in the serum levels of tumor markers as CEA, CA15-3. Computed tomography demonstrated a breast tumor measuring 10 cm. While a slight invasion of the tumor to the pectoralis major muscle was observed, the pleura was not involved.

According to the patient's desire to for prompt relief from the symptoms of pain and ill odor, resection of the tumor (Fig. 1b, 1c) and attachment of an artificial dermis (TERUDERMIS) were performed (Fig. 1d).

Once the initial wound healing was achieved 14 days after the resection (Fig. 1e), transplantation of the skin was performed using an autologous graft (Fig. 1f), and complete healing of the wound was achieved 40 days later (Fig. 1g). Thereafter, additional dissection of axillary lymph nodes was performed, which showed those were not found not involved by metastatic cancer cells.

The patient has begun oral intake of an aromatase

Table 3 Outcome and current condition of the patients

Patients	Operative Time (min)	Additional therapy	Period after operation	Dead or alive
1	54	ALND, AI	3Y7M	Alive
2	68	ALND, AI	2Y5M	Alive
3	95	None	1Y9M	Dead

ALND; Axillary lymph node dissection, AI; Aromatase inhibitor

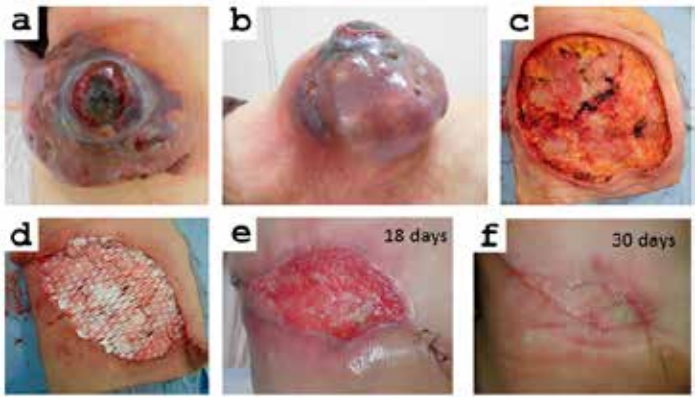

Fig. 2 Operative findings in Case. 2
a, b: A huge tumor measuring 10 cm was found on the right breast with hemorrhage and skin ulceration.
c: Chest wall after dissection of the tumor.
d: An artificial dermis (TERUDERMIS) was attached.
e: Wound 18 days after attachment of the artificial dermis with a favorable wound healing.
f: Complete healing of the wound was achieved 30 days after autologous skin transplantation.

inhibitor and she has been living for three years without any symptoms of tumor recurrence in a favorable physical and mental state.

DISCUSSION

Locally advanced breast cancers (LABC), that have remained untreated due to the patients' neglect or unawareness of cancer occurrence, have led to serious concerns for both patients and physicians. The former involves the clinical symptoms of pain and hemorrhage due to ulceration of the skin, terrible drainage and ill smell due to infection, and mental disorder due to social isolation. The latter comprises the difficulties in selecting and performing therapeutic options, whether or not the patients have incurable factors, such as distant metastasis and broad nodal metastasis.

Patients with LABC, who have been suffering from severe symptoms, are occasionally enthusiastic to undergo surgical treatment rather than drug-induced therapies in order to immediately in order to alleviate the enormous distress and to escape from the symptoms that are adversely impacting their quality of life. For these cases, whether or not the subsequent survival of the patients would be prolonged, restoration of the quality of patients' lives should be mandatory.

LABC has not previously considered to be indicated for treatment with chest wall re-construction. The medical reasons for this contraindication include the higher risk, the possibility of local tumor recurrence, prevention and delay of chemotherapy and/or hormonal therapy due to prolongation of wound healing, and tissue injuries of the graft caused by subsequent radiotherapy.

However, in some previous reports, the rate of local recurrence and successful treatment with the additional therapies, including chemotherapy and irradiation were not different among patients who underwent chest wall reconstruction [3, 4]. Moreover some previous reports have emphasized that the prognosis of patients with LABC treated with palliative surgery was more favorable than that of patients without tumor excision [5, 6].

Of course, an improvement of quality of life might be expected after accomplishing resection of the tumor. Reconstruction to fill up the defect of the skin after surgical dissection of locally advanced breast cancer has been or is now occasionally performed by means of latissimus dorsi flap [7] and transverse rectus abdominis muscle flap [8]. However, these maneuvers are both exceedingly harmful for the patients and also hard for the surgeons.

From this point of view, we attempted to apply a less-invasive maneuver for such patients, and therefore focused on the application of an artificial dermis instead of an autologous muscle flap that would elicit considerable surgical stress.

The artificial dermis consists of collagen, proteoglycans, and elastic fibers. It has been used to prevent scar formation and promote dermal tissue formation, thereby preventing scar contracture [9]. The excellent ability of this medical material for tissue regeneration can be exerted by several factors, including the chemical composition. Terudermis (Terum, Tokyo, Japan) is an artificial dermis with thickness of 3 mm and pore

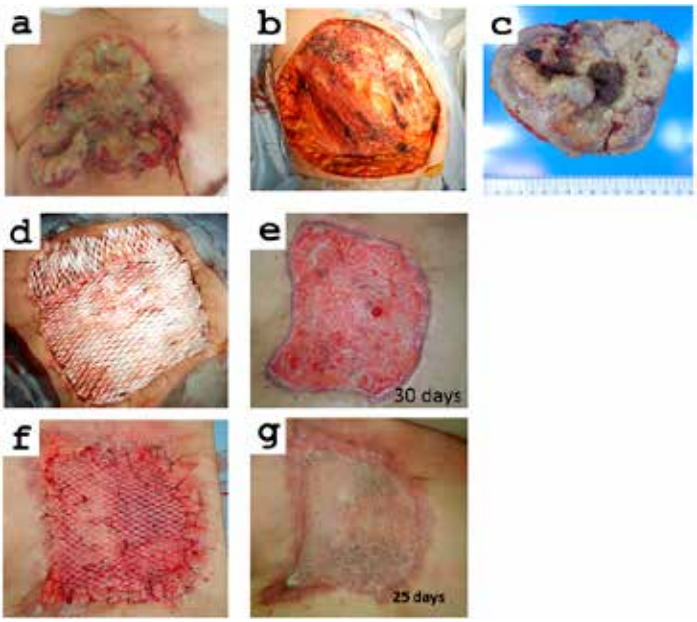

Fig. 3 Operative findings in Case. 3
a: A huge irregular-shaped tumor measuring 13 cm was found on the right breast with hemorrhage and infected drainage.
b: Chest wall after dissection of the tumor.
c: Dissected tumor.
d: An artificial dermis (TERUDERMIS) was attached.
e: Wound 30 days after attachment of the artificial dermis, showing favorable wound healing.
f: Skin transplantation using an autologous graft was performed.
g: Complete healing of the wound (25 days after skin transplantation).

size of 100 micro-meter composed of collagen sponge reconstituted form heat-denatured bovine dermal type 1 collagen [10, 11]. There was no head-to-head clinical study investigating the result of graft skin quality, durability, and vascularization difference between Terudermis and other dermal substitutes. However, a recent experimental investigation demonstrated that Terudermis showed the none-inferior result regarding wound contraction and scar formation compared with other dermal [11].

Therefore, we have come to select Terudermis (Terumo, Tokyo, Japan) as an available and reliable dermal substitute that can be used to replace lost dermis after mastectomy with a simple procedure prior to autologous skin graft transplant. It can both provide tissue volume and a foundation basis to which the autologous skin graft can be subsequently adhere and grow. Accordingly, we could reduce the surgical stress and invasiveness, and to eventually guarantee the quality of life of the patients with LABC.

Such a surgical treatment that might often be palliative for the patients should be as minimally invasive as possible. While the mean operative period in this series of cases was 70 minutes, this surgical maneuver might not be considered excessive.

To the best of our knowledge, regarding clinical usage of dermal substitute in breast surgery, there is one recent clinical report demonstrating an available application of dermal substitute after mastectomy for a huge phyllodes tumor of the breast [12].

Among the therapeutic option, some drug therapies, including hormonal therapy and chemotherapy, were initially suggested for patients with LABC [13, 14], which has lead the patients to seek tumor reduction through a less-invasive surgical treatment without muscular replacement in order to fill the defect of the chest wall. However, the patients commonly requested to undergo immediate surgical dissection of the tumor, despite considerable physical invasiveness in order to escape the distressing associated symptoms, including pain, hemorrhage, odor, and also fear.

One patient (Case 3), who had been living under a comparatively favorable condition, escaping the distress of severe pain, bleeding and ill-smell brought about by the fungating tumor that afflicted her, died of progression of metastatic brain tumors 21 months after the surgical treatment. Two patients who also avoided the severe symptoms have been alive for 43 months and 29 months, respectively, under a satisfactory condition without signs of tumor recurrence.

Documentation of the current cases can demonstrate the clinical usefulness of mastectomy and replacement using artificial dermis for patients with locally advanced breast cancer suffering from distressing symptoms that adversely impact their quality of daily life.

From our clinical experience, regular indications for a reconstruction using attachment of artificial dermis after total resection for locally advanced breast cancer have been suggested as follows.:

1. Although no limitation on the age of the patient is defined, general physical condition tolerable for general anesthesia and an operation taking three hours can be guaranteed.
2. Pleura and thoracic organs are not involved or invaded by the breast tumor.

3. Improvement of the quality of life by the dissection of the tumor causing such symptoms as pain, hemorrhage, and odor, would be expected.

However, this surgical procedure would not be indicated for all patients with LABC and the medical indication and rational for the treatment should be further discussed more absolutely and thoroughly.

CONFLICT OF INTEREST

Authors declare that we have no financial interest or conflict of interest.

REFERENCES

1) Hamashima C, Hattori M, Honjo S, Kasahara Y, Katayama T, Nakai M, *et al*. Japanese Research Group for the Development of Breast Cancer Screening Guidelines. Jpn J Clin Oncol 2016; 46: 482–92.
2) Tohno E, Umemoto T, Sasaki K, Morishima I, Ueno E. Effect of adding screening ultrasonography to screening mammography on patient recall and cancer detection rates: a retrospective study in Japan. Eur J Radiol 2013; 82: 1227–30.
3) Howard MA, Polo K, Pusic AL, Cordeiro PG, Hidalgo DA, Mehrara B, *et al*. Breast cancer local recurrence after mastectomy and TRAM flap reconstruction: incidence and treatment options. Plast Reconstr Surg 2006; 117: 1381–6.
4) Newman LA, Kuerer HM, Hunt KK, Kroll SS, Ames FC, Ross MI, *et al*. Presentation, treatment, and outcome of local recurrence afterskin-sparing mastectomy and immediate breast reconstruction. Ann Surg Oncol 1998; 5: 620–6.
5) Veronesi G, Scanagatta P, Goldhirsch A, Rietjens M, Colleoni M, Pelosi G, *et al*. Results of chest wall resection for recurrent or locally advanced breast malignancies. Breast 2007; 16: 297–302.
6) Pan H, Zhang K, Wang M, Ling L, Zhou W, Wang S. Palliative local surgery for locally advanced breast cancer depending on hormone receptor status in elderly patients. Clin Breast Cancer 2019; 19: 247–60.
7) Munhoz AM, Montag E, Arruda E, Okada A, Brasil JA, Gemperli R, *et al*. Immediate locally advanced breast cancer and chest wall reconstruction: surgical planning and reconstruction strategies with extended V-Y latissimus dorsi myocutaneous flap. Plast Reconstr Surg 2011; 127: 2186–97.
8) Martella S, Caliskan M, Brenelli FP, Rossetto F, De Oliveira HA, Lima LN, *et al*. Surgical closure of chest wall in noninflammatory locally advanced breast carcinoma with ulceration of the skin. Breast J 2008; 14: 345–52.
9) Hatoko M, Kuwahara M, Tanaka A, Tada H, Yurugi S, Mashiba K, *et al*. Application of artificial dermis graft to correct a depression after tissue resection. Ann Plast Surg 2000; 45: 633–40.
10) Eo S, Kim Y, Cho S. Vacuum-assisted closure improves the incorporation of artificial dermis in soft tissue defects: Terudermis and Pelnac. Int Wound J 2011; 8:261–7.
11) Hori K, Osada A, Isago T, Sakurai H. Comparison of contraction among three dermal substitutes: morphological differences in scaffolds. Burns 2017; 43: 846–51.
12) Abe H, Teramoto A, Takei Y, Tanaka Y, Yoneda G. Malignant phyllodes tumor of the breast with rapid progression: a case report. Surg Case Rep. 2020; 6: 308.
13) McIntosh SA, Ogston KN, Payne S, Miller ID, Sarkar TK, Hutcheon AW, *et al*. Local recurrence in patients with large and locally advanced breast cancer treated with primary chemotherapy. Am J Surg 2003; 185: 525–31.
14) Spanheimer PM, Carr JC, Thomas A, Sugg SL, Scott-Conner CEH, Liao J, *et al*. The response to neoadjuvant chemotherapy predicts clinical outcome and increases breast conservation in advanced breast cancer. Am J Surg 2013; 206: 2–7.