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].
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 carcinomatapillotubular 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
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

Table 1. Formulation of Mohs’ paste

| Material                           | Original method [3,7] | Our hospital |
|-----------------------------------|-----------------------|--------------|
| Saturated zinc chloride           | 34.5 mL               | 25 g         |
| Zinc chloride                     |                       |              |
| Purified water                    |                       | 15 mL        |
| Powdered Sanguinaria canadensis   | 10 g                  |              |
| Zinc oxide starch powder          |                       | 30 g         |
| Paste containing stibnite         | 40 g                  |              |
| Glycerin                          |                       | 15 mL        |
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].
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 | Reconstruct- | Adverse events | Outcome | Ref |
|------|--------------|----------|-----------|---------------|------|-------|--------------|-----------------|-------------------------------|----------|-----------------|------------|---------------|---------|-----|
| 1    | 59/F         | Bleeding, exudate, stink | Scirrhous, 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 | Scirrhous, 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    | 40/F         | Bleeding, exudate, stink, respiratory discomfort | X | -/+/- | 4b 2 1 IV | + | - | 90 | PR | - | - | - | Improved | 11 |
| 5    | 52/F         | Bleeding, exudate, stink | G-CSF producing, squamous cell carcinoma, Scirrhous, invasive ductal carcinoma | +/-/- | 4b 3 1 IV | + | - | 1 | PR | - | - | Bleeding | Died 11 months later | 12 |
| 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 X | X | X | 1 | PR | X | X | - | Improved | 16 |
| 10   | 70/F         | Bleeding, exudate, stink | Scirrhous, 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 | Scirrhous, 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, stink | Invasive ductal carcinoma | -/+/- | 4b 2 1 IV | + | - | 6 | PR | - | - | - | Improved | 20 |
| 15   | 77/F         | Bleeding, exudate | X | X | X X X X X X X | X | X | 30 | PR | - | - | - | NA | 21 |
| 16   | 56/F         | Bleeding, exudate, stink | 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)
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

### 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 | Chemotherapy | Hormonal therapy | The day of improved symptoms (days) | Response | Salvage operation | Reconstructive surgery | 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, stink | X | +/-/+ | 4 | 1 | 4 | IIIIB | X          | -              | 1                   | PR       | -                | -                 | -               | 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 | 0 | 1 | IIIIB | X          | 1              | PR                  | -        | -                | -                 | Died 2 months later | 29    |
| 25   | 68/F     |     | Bleeding | X | +/-/+ | 4c | 0 | 1 | IIIIB | +          | +              | 30                  | CR       | +                | Split skin graft | -               | Improved | 30  |
| 26   | 49/F     |     | Bleeding | X | X | 4b | 1 | 1 | IV    | +          | -              | 14                  | PR       | +                | -                 | -               | Improved | 31  |
| 27   | 64/F     |     | Bleeding, exudate, stink | X | X | X | X | X | X | X | + | - | 455                  | PR | - | - | Improved | 31 |
| 28   | 55/F     |     | Bleeding, exudate, stink | X | X | X | X | X | X | X | + | - | 60                  | PR | + | X | X | Improved | 31 |
| 29   | 90/F     |     | Bleeding, exudate, stink | X | 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, stink | Invasive ductal carcinoma | +/-/+ | 4c | 0 | 0 | IIIIB | + | - | 30                  | PR | - | - | - | Improved | 34 |
| 33   | 68/F     |     | Bleeding, exudate | Mucinous carcinoma | +/-/- | 4b | 0 | 1 | IIIIB | + | + | 2                  | PR | + | Split skin graft | Pain | Improved | 35 |
| 34   | 66/F     |     | Bleeding, exudate, stink | Invasive ductal carcinoma | -/-/- | 4b | 1 | 0 | IIIIB | + | - | 1                  | PR | + | Split skin graft | - | Improved | 36 |
| 35   | 50/F     |     | Bleeding, exudate, stink | Scirrhous, invasive ductal carcinoma | +/-/+ | 4 | 3 | 1 | IV | - | + | 10                  | CR | - | - | - | Died 9 months later | 37 |
| 36   | 40/F     |     | Bleeding, exudate | Scirrhous, invasive ductal carcinoma | -/-/- | 4 | 2 | 1 | IV | + | - | 32                  | PR | - | - | - | Improved | 37 |
| Our case | 64/F |     | Bleeding, exudate, stink | Papillotubular carcinoma | +/-/- | 4b | 1 | 0 | IIIIB | + | - | 2                  | PR | + | Latissimus dorsi musculocutaneous 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.
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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