Original

Efficacy of Micrografting Strategy for Abdominal Refractory Skin Ulcer Associated with SSI

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Abstract

Introduction: The micrograft technique involves collecting a small amount of healthy tissue which is then disaggregated and transplanted to cover a larger wound area. We present our experiences and findings utilizing micrografts for abdominal wound dehiscence associated with postoperative gastroenterological surgical site infections (SSIs).

Materials and Methods: This is a retrospective study constructed from medical records including patient backgrounds, gastroenterological diagnosis, wound culture results, duration of epithelialization, and adverse events. Patients whom have undergone micrograft treatments for abdominal wound dehiscence associated with postoperative gastroenterological SSIs were considered for the study. The micrograft procedure was performed under local anesthetics using the Rigenera® system based on its protocol.

Results: All 4 cases are presented below. Of the total cases, 3 patients were accompanied by septic shock associated with acute panperitonitis after emergency laparotomy. Two cases had positive MRSA bacterial culture results. In all cases, the wounds healed, no adverse events were observed, and no limitations on postoperative activities.

Case 1: A 68-years-old male patient with peritoneal metastasis of unknown primary site and small-intestinal perforation. Epithelialization was observed 3 weeks after the micrograft treatment. The patient was discharged from the hospital 4 weeks after the micrograft treatment.

Case 2: Male patient, 79-years-old, with a small-intestinal perforation associated with liver cancer surgery. Hospital discharge at 6 weeks after the micrograft treatment and epithelialization of the ulcer was observed at 8 weeks postoperatively.

Case 3: A 59-years-old female patient, diagnosed with colonic perforation penetrating into the abdominal wall, forming an abdominal wall abscess. The patient was discharged approximately 4 weeks from the micrograft procedure.

Discussion: The autologous tissue is minced into pieces of 50 to 70 μm using the Rigenera® system, and the tissue suspension is then transplanted. The procedure can be performed under local anesthetics, allowing patients with general anesthetic considerations to receive the treatment. Restrictions on postoperative activities were considered to be unnecessary after micrografting, and patients were able to start postoperative rehabilitation without any limitations.

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—Key words—

micrograft, SSI, refractory skin ulcer

Introduction

In a micrograft technique, a small amount of healthy skin and subcutaneous tissue are collected, disaggregated into sizes from several mm to tens of μm, and transplanted to a larger area than the donor site[1)]. The first

transplantation method was originated by Reverdin and published in 1869[2], which was succeeded by many others with various ingenuities[3)–7)]. In recent years, micrograft is receiving more attention as a new and less-invasive treatment strategy for wound healing, but not much has been reported to date on its effect pertaining to refractory skin ulcers[8)–11)]. We have experienced cases of wound dehiscence due to postoperative wound infection associated with emergency laparotomy for acute panperitonitis. The physical conditions of each patient were considered to be hard-to-treat; nevertheless, the micrograft technique showed good results. Only one previous study[12] was found on micrograft-treated cases involving skin ulcers associated with postoperative SSIs, and we have presented here some findings based on the treatments.

Materials and Methods

The study was conducted with the approval (approval number: 2020002) by the Ethics Committee of Kitasato University Medical Center. Patients whom have undergone micrograft treatments on abdominal wound dehiscence associated with postoperative gastroenterological SSIs were considered for the study. This study was retrospectively constructed from medical records, including patient backgrounds, gastroenterological diagnosis, wound culture results, the duration of epithelialization, and adverse events. All micrograft procedures were performed under local anesthesia.

Micrograft preparation and transplantation:

The micrograft preparation method shown in Fig. 1 is referenced from our reported study in year 2022[13]. Micrograft suspension was created based on the protocol for the Rigenera® system (HBW srl, Italy). A spindle-shaped sample of approximately 4 × 2 cm in size was harvested from the abdomen as donor site. The harvested skin was divided into layers of (1) epidermal–upper dermal layer and (2) mid-dermal–subcutaneous layer. The donor site wound was closed with a suture. Harvested tissue fragments (1) (2) were prepared separately. Consequently, micrograft suspensions (1) and (2) were generated independently. The system's disaggregation device Rigeneracons® comes in sizes of 2 ml and 16 ml. An appropriate device is selected based on the wound size. The harvested sample is cut into fragments of 2 to 3 mm which are then placed inside the Rigeneracons® with saline solution of 2 mL or 16 mL. Micrograft suspension is created by placing the device on the Rigenera® machine and disaggregating for approximately 2 minutes. The suspension is dispensed into a 1 ml syringe. Before transplantation, the ulcer is debrided, cleansed and sprayed with bFGF (Kaken Pharmaceutical Co., Ltd., Japan). At first, micrograft suspension (2), the dermal–hypodermal layer, was injected using a 27 G needle into the ulcer and at its edges, infused within the subcutaneous layer at approximately 1 cm intervals in a grid pattern. Nextly, micrograft suspension (1), the epidermal–upper dermal layer, was sprayed onto the ulcer surface, or was used to infiltrate an artificial dermis made from collagen sponge and silicon film (Pelnac Gplus®, Gunze Limited, Japan) and transplanted to the ulcer. For cases where the graft suspension was sprayed, Sofratulle® Gauze Dressing (Teika Pharmaceutical Co., Ltd., Japan) was used; for other cases that employed the artificial dermis, preoperative treatments were continued. All procedures took place at the treatment room within the ward area, under local anesthesia.

Results

The study consisted of a total of 3 cases, with patient ages between 59 to 79 years. A detailed summary of the cases is provided under Table 1. In all cases, patients were admitted to ICU during the clinical course of the disease, and 3 cases reported septic shock after gastroenterological surgery. In 3 cases, wound depth reached the peritoneum, and in one case, the wound reached as far as the intestines. Prior to the micrograft treatment, 2 patients had positive MRSA wound culture results. In all cases, no restrictions were prescribed for postoperative activity, and they all continued with functional rehabilitation. Prior to micrograft treatments, in all the cases, negative pressure wound therapy installation and dwelling (NPWT-id) was applied on the wounds, which continued after the micrograft treatments. Of the cases, 3 patients required no additional surgery and, in one case, a patch graft was used to heal the wound. No adverse events were reported. Summary of each case follows.

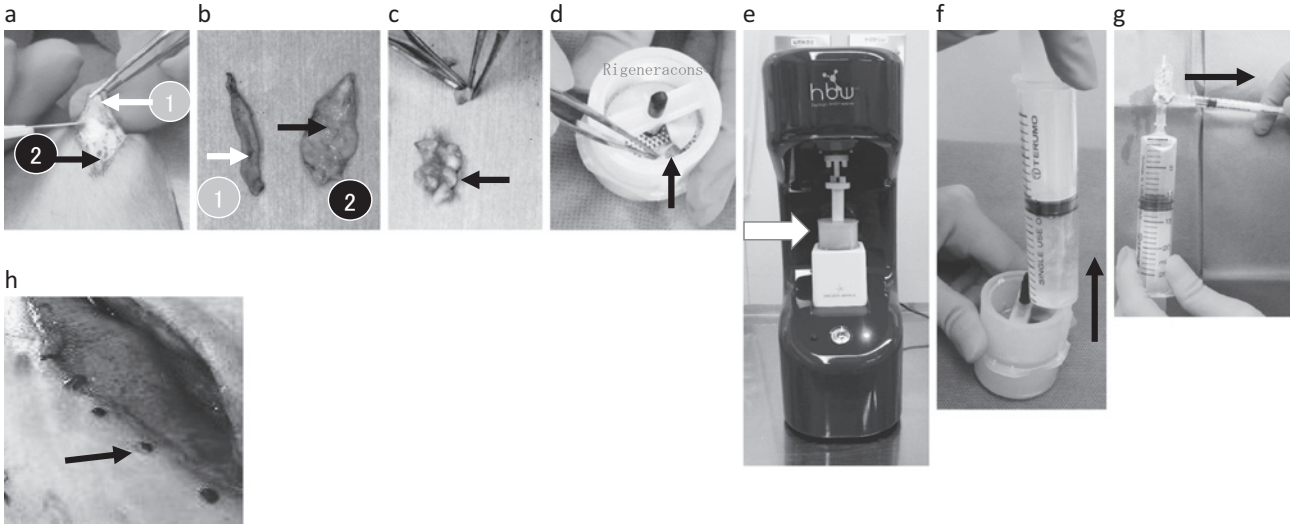

Fig. 1 Micrograft Preparation (referenced from Niimi et al., 2002[5])

a. Epidermal – upper dermal layer (e; white arrow) was harvested. Black arrow indicates the mid-dermal layer. Mid-dermal – hypodermal layer (D; black arrow) was harvested.
b. Harvested samples of epidermal – upper dermal layer (E; white arrow) and mid-dermal – hypodermal layer (d; black arrow) are shown.
c. Mid-dermal – hypodermal layer was cut into pieces of approximately 2 to 3 mm with a surgical blade.
d. Skin tissue fragments (black arrow), each piece 2 to 3 mm in size, were placed inside the Rigeneracons®.
e. Saline solution was added to the Rigeneracons® and the device was then placed on the Rigenera® machine in order to disaggregate the samples.
f. Micrograft suspension was collected from the Rigeneracons®.
g. The suspension is dispensed into a 1 ml syringe (black arrow).
h. Micrograft suspension D, the dermal – hypodermal layer, was injected into the ulcer and at its edges (black arrow), infused within the subcutaneous layer at approximately 1 cm intervals in a grid pattern.

Table 1 Table summarizing patient data for the 3 cases in our study.

Case No.	Age	Gender	Main Medical History	Surgical diagnosis	Systemic condition at the time of surgery	Wound depth before micrograft treatment	Main wound culture results	Additional surgery	Combination therapy	Duration of epithelialization after micrograft treatment	Period to hospital discharge post-micrograft	Period to hospital discharge post- micrograft
1	68	M	Hypertension	Colonic perforation after surgery for cancer of unknown primary, peritonitis	Septic shock	On the peritoneum	MRSA	None	NPWTid	3 weeks	3 weeks	4 weeks
2	79	M	Diabetes	Small intestinal perforation after liver cancer surgery, peritonitis	Septic shock	On the peritoneum	MRSA	Patch graft	NPWTid	8 weeks	8 weeks	6 weeks
3	59	F	Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)	Colonic perforation, abdominal wall abscess	Septic shock	Intestines	E.coli	None	NPWTid	4 weeks	4 weeks	4 weeks

Case 1 (Fig. 2):

Male, 68 years-old with peritoneal metastasis of unknown primary site and small-intestinal perforation. Comorbidities: hypertension and hyperlipidemia. Past medical history: varicose veins on the lower limbs.

History of present illness: The patient had septic shock and was transported by ambulance to our hospital. An emergency laparotomy was performed for the acute panperitonitis, followed by closure of the perforated site and ileostomy with double orifices. The cause of the colonic perforation was diagnosed as the peritoneal metastasis of unknown primary site. SSI occurred 1 week after the emergency laparotomy. Abdominal incision dehiscence occurred due to the SSI, forming an ulcer which tested positive for MRSA. Because of the ulceration at the abdominal midline, stomal construction became a challenge, and 2 weeks post-op, the patient was referred to our department.

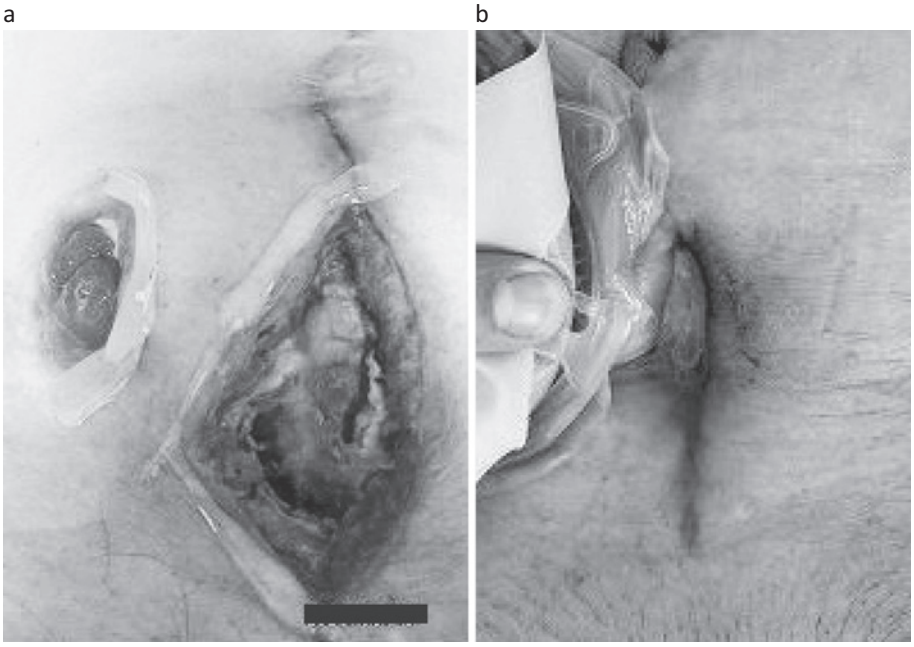

Fig. 2 Wound area for Case 1
a. Condition before the micrograft treatment.
b. Conditions after the treatment and during healing.

Postoperative course: The patient had advanced cancer with a life expectancy of a few months. The patient and his family wished for an early discharge. NPWT-id was applied to improve the wound bed environment, and 2 months after the surgery, micrograft procedure was conducted. The tissue suspension was prepared using the dermis, which was transplanted into the ulcer and at its margins. Likewise, another tissue suspension using the epidermis was prepared and transplanted to the ulcer surface. The ulcer area had mostly epithelialized approximately 3 weeks after the micrograft treatment, and the stoma became easier to manage. The patient was discharged approximately 4 weeks (about 3 months from the initial surgery) after the micrograft treatment.

Case 2 (Fig. 3):

Male, 79 years-old, diagnosed with small-intestinal perforation associated with liver cancer surgery. Comorbidities: hepatic cirrhosis, diabetes and hypertension. Past medical history: subarachnoid hemorrhage, cerebral aneurysm surgery, bladder cancer surgery, and esophageal cancer radiation therapy.

History of present illness: A small-intestinal perforation was detected after laparoscopic hepatic subsegmentectomy for the hepatic cancer. An emergency laparotomy was performed due to the acute panperitonitis successively with septic shock. SSI occurred 5 days post-op from the emergency laparotomy which was followed by dehiscence of the abdominal midline incision. The wound base showed a defect in the peritoneum, developing a 15 cm ulcer pocket on the right side which tested positive for MRSA. Our department has intervened two weeks into the initial surgery.

Postoperative course: This was a case of an elective surgery with postoperative complications, in which an early discharge was desired after the surgical treatments. NPWT-id was applied to promote formation of granulation tissue at the defective peritoneal region, which improved the wound bed environment. The micrograft treatment occurred at 1.5 months after the initial surgery. Tissue suspension was prepared using the dermis, and transplanted inside the ulcer and at its margins. The epidermal sample was 5 mm in size and was transplanted onto the surface of the ulcer. Approximately 6 months from the micrograft procedure, self-treatment of the wound became possible and the patient was discharged. Full epithelialization was observed approximately 8 weeks from the micrograft treatment.

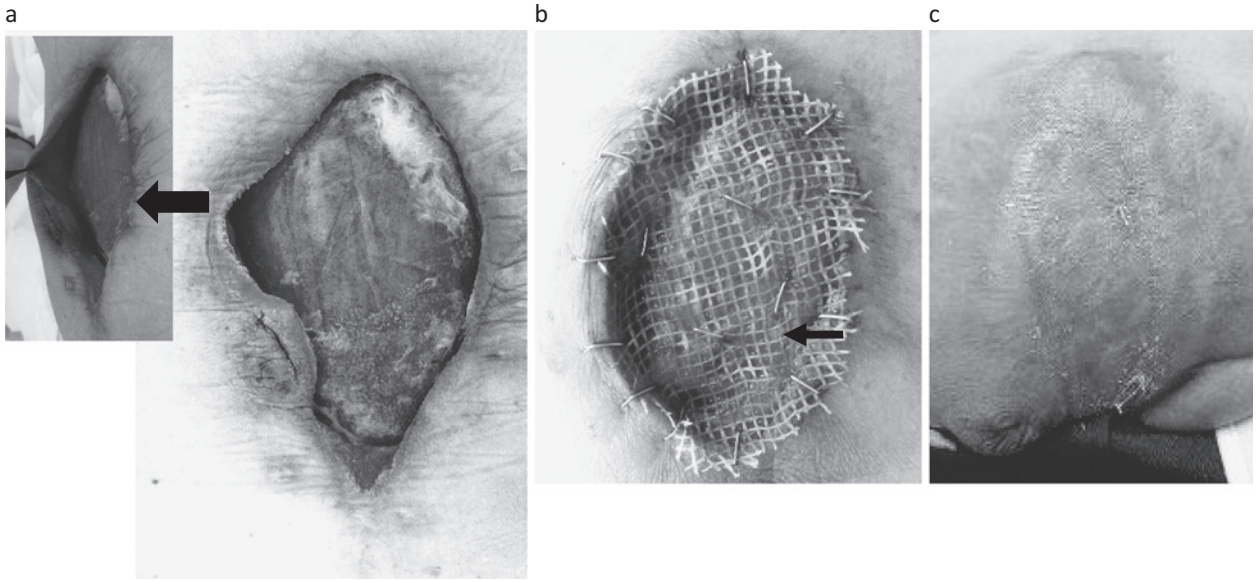

Fig. 3 Wound area for Case 2
a. Condition before the micrograft treatment.
b. Conditions after the patch graft.
c. Conditions after the treatment and during healing.

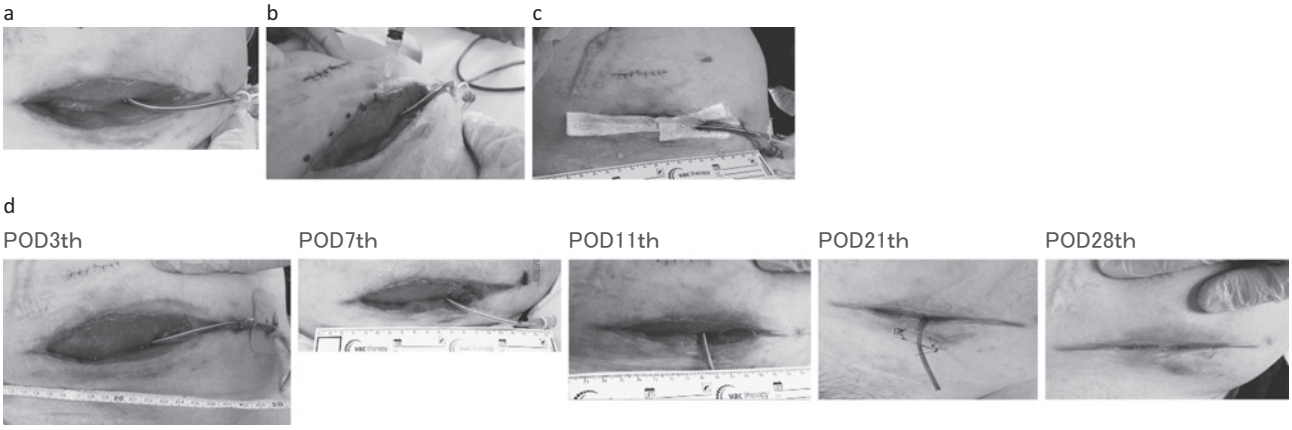

Fig. 4 Wound area for Case 3
a. Condition before the micrograft treatment.
b. Micrograft suspension D was injected into the ulcer and at its edges.
c. Micrograft suspension E which was then infiltrated into an artificial dermis (Pelnac Gplus®, Gunze Limited, Japan) and transplanted to the surface of the ulcer.
d. Conditions after the treatment and during healing.

Case 3 (Fig. 4):

Female, 59 years-old, diagnosed with a colonic perforation penetrating into the abdominal wall, forming an abdominal wall abscess. Comorbidities: chronic inflammatory demyelinating polyradiculoneuropathy (with long-term steroid use), hyperlipemia, hypertension and obesity. Past medical history: colonic perforation associated with colostomy.

History of present illness: The patient was transported to the hospital emergency department due to abdominal pain and emesis. Detailed examinations found that the patient had a recurrence of colonic perforation, which penetrated into the abdominal wall, forming an abdominal wall abscess and cellulitis, which eventually lead to septic shock. The patient underwent emergency operation (debridement) at the surgical department. For the open wound abscess, a catheter was inserted into the intestine for drainage of intestinal fluids. The aim

was to manage it as an enterocutaneous fistula, but it had developed into an infected wound due to leakage of intestinal fluids around the catheter. Our department intervened at 2 weeks post-op from the first surgery.

Postoperative course: With the application of NPWT-id, the wound bed environment improved and the first micrograft treatment was performed 1 month postoperatively. The tissue suspension prepared from the dermis was transplanted inside the ulcer and its border. Similarly, another tissue suspension was created using the epidermis which was then infiltrated into an artificial dermis (Pelnac Gplus®, Gunze Limited, Japan) and transplanted to the surface of the ulcer. A catheter for the enterocutaneous fistula spontaneously dislodged and the intestinal fistula closed. No recurrence of the enterocutaneous fistula was observed. At approximately 4 weeks from the micrograft procedure, almost all of the ulcer had closed and the patient was discharged.

Discussion

Micrograft is a treatment method that entails harvesting and disaggregating the autologous skin and hypodermal tissue, and transplanting the micrografts over a larger area. Since it was first reported, various authors have followed with ingenuities including different fragment sizes. Zhang et al. in 1986 reported a method of split-thickness skin graft in which the skin sample is minced into pieces of approximately 1 mm in size, which are then transplanted on the surface of a burn wound[7][14]. The method came to be known and was reacknowledged as a less-invasive method. In 2013, a micrograft system called Rigenera® (HBW srl, Italy) which creates tissue fragments of a size between 50 to 70 μm was developed. Our cases utilized this technique in accordance with its protocol. The method (Fig. 1) involves collecting a skin sample of a few centimeters in size. This technique, however, does not require skin graft fixation as seen in conventional skin transplants. It is a simple procedure conducted under local anesthesia, and also can be performed in cases where the patient's systemic condition is not favorable for general anesthesia. All of our reported cases had comorbidities and required ICU admission, but all patients were able to undergo the micrograft procedure without any issues. Despite the fact that SSIs can cause a considerable burden on clinical resources and be a mental distress to a patient, in all of our cases, the micrograft procedure was performed in the treatment room and was less stressful for all parties involved.

To our knowledge, no reports have been found pertaining to micrograft treatment performed on ulcers associated with SSIs. In our study, the micrograft treatment was applied in an environment where no apparent infections are present through wound bed preparation, including infected granulation tissue and necrotic tissue debridement and suture removal. Not only control of the infection itself, but underlying comorbidities were adequately treated prior to the micrograft procedure. In view of the fact that full epithelialization necessitates a certain amount of time after a micrograft procedure, continual and adequate postoperative wound management was indispensable. Even when an SSI tested culture positive for bacterial infection, as long as there was adequate infection control, micrograft procedure was considered to be useful.

Despite the ulcers being considered as difficult-to-treat, all cases nonetheless formed apparent granulation after the micrograft treatment. Even with the NPWT-id application, micrograft treatments were perceived to be effective each time. General observation showed that granulation tissue formed on the whole ulcer, indicating an elevation of the ulcer's base and a size reduction of the wound width, followed by epithelialization from the surrounding edges. Case 2 consisted of a wound with large epidermal loss, and a patch graft was used to compensate for the epidermal cells in order to encourage epithelialization. In our past reports pertaining to micrograft treatments, epithelialization was not demonstrated as forming islands within the ulcer area. We reported that chemical mediator asocciated whith micrograft could promote wound healing rather than the micrograft itself attachment[13]. Therefore, in Case 2, we decided that a patch graft was performed due to size of skin-lack.

It is generally known that the wound healing goes through hemostasis, inflammation, proliferation and remodeling phases in which various cells are activated; in addition to these cells, cytokines and growth factors are identified as playing an important role[14)–17)]. In conventional skin grafting, new blood vessels are initially formed from the transplant/recipient bed to the grafted tissue, allowing the grafted tissue to adhere to the transplant/recipient bed. On the other hand, the mechanism of micronized tissue transplantation, although

clinically still unclear, is presumed to be different from the traditional approach. Micrograft suspension created by the Rigenera® system has been reported in various studies such as in vitro experiments using human tissue[1] as well as in vivo mice experiments[15][16]. These studies suggested that cytokines and growth factors within the micronized tissue fragments may have induced a beneficial physiological response to heal wounds. In 2022, we have presented our histological analysis of clinical samples based on the use of the Rigenera® system[13]. Our hypothesis at the time was not in contradiction with earlier studies reported by various authors[15][16]. Conventional skin graft requires a few days for the blood vessels to form from the transplant/recipient bed to the graft tissue; during this time, the patient is prescribed postoperative bed rest to allow the skin graft to be in close contact with the transplant/recipient bed until it stabilizes. In other words, bed rest may compromise mobility, leading to a decline in activities of daily living (ADL). Conversely, because the transplanted tissue is smaller when using the micrograft and with the understanding that physiological response is key to its efficacy, we surmised that a bed rest would be unnecessary. Our micrograft cases demonstrated that the ulcers improved even without any rehabilitation limitations and ADL recovery was not impaired, contributing to shortening the length of hospital stay. The micrograft treatment was beneficial for inpatients with concerns pertaining to limitations on postoperative rehabilitation.

Limitations

The number of cases were limited in this study. Additionally, the study was based on clinical cases and there was difficulty of arranging for a control group. As such, a comparative investigation was not considered.

Conclusion

The study presents cases of micrograft treatment performed on wound dehiscence associated with postoperative gastroenterological SSIs. The less-invasive micrograft procedure demonstrated to be beneficial in healing skin ulcers associated with SSIs for patients with unfavorable systemic conditions.

References

1) Sato S: Role of cell adhesion molecules in wound healing. Jpn J Clin Immun 24 (3): 98—111, 2001.
2) Reverdin JL: Graffe epidermique. Experience faite dans le service de M. le docteur Guyon, a l'hopital Necker. Bull Imp Soc Chir Paris 10: 511—515, 1869.
3) Zhang ML, Wang CY, Chang ZD, et al: Microskin grafting. II. Clinical report. Burns Incl Therm Inj 12 (8): 544—548, 1986.
4) Singer AJ, Clark RA: Cutaneous wound healing. N Engl J Med 341: 738—746, 1999.
5) Niimi Y, Baba K, Tsuchida M, Takeda A: A Histological Evaluation of Artificial Dermal Scaffold Used in Micrograft Treatment: A Case Study of Micrograft and NPWT Performed on a Postoperative Ulcer Formation after Tumor Resection. Medicina (Kaunas) 58 (1): 73, 2022.
6) Gurtner GC, Werner S, Barrandon Y, Longaker MT: Wound repair and regeneration. Nature 453: 314—321, 2008.
7) Barrientos S, Stojadinovic O, Golinko MS, et al: Growth factors and cytokines in wound healing. Wound Repair Regen 16: 585—601, 2008.
8) Trovato L, Monti M, Del Fante C, et al: A new medical device Rigeneracons allows to obtain viable micro-grafts from mechanical disaggregation of human tissues. J Cell Physiol 230: 2299—2303, 2015.
9) Jimi S, Kimura M, De Francesco F, et al: Acceleration mechanisms of skin wound healing by autologous micrograft in mice. Int J Mol Sci 18: E1675, 2017.
10) De Francesco F, Graziano A, Trovato L, et al: A regenerative approach with dermal micrografts in the treatment of chronic ulcers. Stem Cell Rev and Rep 13: 139—148, 2017.

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腹部 SSI による難治性皮膚潰瘍に対する micrograft 治療の有用性

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—キーワード—
マイクログラフト（micrograft），術後創感染（SSI），難治性皮膚潰瘍

緒言：micrograft は少量の健常組織を採取し細断してより広範囲の面積に移植する治療法である．我々は消化器術後創感染（SSI）による腹部離解創に micrograft を用いて良好な結果を得た症例を経験し，知見を得たため報告する．

対象と方法：消化器術後創感染（SSI）による腹部離解創に対し，micrograft を用いた症例を検討した．診療録をもとに，患者背景，消化器外科診断名，創細菌培養結果，上皮化までの期間，有害事象，術後管理を後ろ向きに検討した．micrograft は局所麻酔下に，RIGENERA システム®を用いて，そのプロトコールに準じて施行した．

結果：全 3 例は急性汎発性腹膜炎で敗血症性ショックとなり緊急開腹手術後であった．2 例に創細菌培養で MRSA を検出した．全例で創は治癒した．全例で創部管理目的の安静制限は行わずリハビリテーションを術後も継続した．有害事象は認めなかった．

症例 1：68 歳男性．原発不明癌腹膜播種・小腸穿孔．micrograft 施行の約 3 週間後に創は上皮化し，micrograft 施行 4 週間後に退院した．

症例 2：79 歳男性．肝臓癌術後小腸穿孔．micrograft 施行の約 6 週間後に退院，micrograft 施行約 8 週間後に潰瘍は上皮化した．

症例 3：59 歳女性．結腸穿孔の腹壁穿通，腹壁膿瘍．micrograft 施行の約 4 週間後に創は上皮化し，退院した．

［COI 開示］本論文に関して開示すべき COI 状態はない

（日職災医誌，73：10—17，2025）