need for immediate surgery to evaluate the differences in the status of wounds between patients with chronic renal failure (CRF) due to DM and that due to other diseases. All information was obtained from patients' medical records, examination, and interview at the first examination.

Patients receiving HD because of DM (57%) ranged in age from 53 to 74 years (mean age, 62.4 ± 7.9 years), and patients receiving HD because of other diseases, including chronic glomerular nephritis, polycystic kidney, and systemic lupus erythematosis (43%), ranged in age from 52 to 69 years (mean age, 61.3 ± 6.0 years) (no significant difference, Wilcoxon's rank-sum test). We investigated differences in the cause of wounds and in the time between the development of wounds after the start of HD in patients with CRF due to DM or other diseases. Statistical analysis was performed using Student's t-test.

RESULTS

The patients' originated diseases, characteristics of wounds, the interval between the start of HD to the development of the wounds, and complications are shown in Table 1.

All diabetic patients were classified as having type 2 DM. Wounds in patients with CRF due to DM were caused due to ischemia in 2 cases (25%), trauma (burn and pressure ulcer) in 2 cases (25%), and infection in 4 cases (50%). On the other hand, wounds in patients with CRF due to other diseases were associated with ischemia in 2 cases (33%) and trauma in 4 cases (67%).

Methicillin-resistant *Staphylococcus aureus* (MRSA) were isolated from 7 of 8 chronic wounds in patients with DM, and 2 of 6 chronic wounds in patients without DM. Among them, 6 of 7 patients with DM and 1 of 3 without DM required immediate debridement, including amputation.

The mean interval from the start of HD to wound development in patients with CRF due to DM was 3.5 years, and that in patients with CRF due to other diseases was 12.9 years. There was a significant difference between the groups (P=0.04).

The serous calcium level of diabetic patients ranged from 7.1 to 9.3 mg/dL (mean, 8.5 ± 0.7 mg/dL), and that of nondiabetic patients ranged from 8.9 to 10.2 mg/dL (mean, 9.6 ± 0.5 mg/dL). There was no significant difference between the groups (P=0.5). The inorganic phosphate level of diabetic patients ranged from 2.4 to 4.2 mg/dL (mean, 3.7 ± 0.6 mg/dL), and that of nondiabetic patients ranged from 2.8 to 4.6 mg/dL (mean, 3.2 ± 0.8 mg/dL). There was no significant difference between the groups (P=0.4).

DISCUSSION

Extremity ulcers in patients receiving HD are often difficult to heal. Nonetheless, patients with severely ischemic limbs due to maintenance HD are markedly increasing in number.[1,2] Amputation of the limb is sometimes performed for these complex ulcers, because patients receiving HD are thought to present with immunocompromised conditions, and aggressive life-threatening infection such as sepsis requires immediate surgical debridement in order to salvage blood access line and their life. On the other hand, surgical amputation is the only way to resurface these wounds, especially, for some ischemic necrosis wounds including total finger or foot dry necrosis. In our cases, 6 patients underwent amputation of the finger or the limb; 5 were due to complicated sepsis and 1 was due to dry necrosis associated with arteriosclerosis obliterans.

It is commonly believed that the development of ischemic limb ulcers in patients with CRF is influenced by underlying advanced diabetic microangiopathy.[3] Although we have investigated severe extremity ulcers that required surgical treatment, the present study indicates that the development of ulcers in patients with DM is not only associated with ischemia but is also strongly influenced by infection, because 7 of 8 patients with DM had infectious conditions such as gangrene, osteomyelitis, and necrotizing fasciitis. On the other hand, the development of ulcers in patients without DM was mainly due to ischemia and trauma. Among them, 2 patients developed MRSA sepsis originating from secondary wound infection, and underwent amputation.

The interval from the start of HD to wound development in patients with DM was significantly shorter than that in patients without DM. Generally, ulcers in patients with CRF and DM are thought to develop because of peripheral neuropathy, which reduces protective sensations.[4] In addition, several investigators have reported that the incidence of peripheral arterial occlusive disease in patients receiving HD ranges from 2.5% to 19.0%.[5,6] Because of these neurovascular disorders, extremity ulcers develop more easily in patients with DM than in patients with other diseases.

These infectious wounds often result in higher mortality rates because blood access shunts, especially when artificial vessels were grafted, are easily infected. Bacteria from the wounds usually diffuse proximally along the

subcutaneous flow of lymph or blood and can cause shunt infections, which cause the loss of blood access channels and life-threatening sepsis. All our patients with infectious wounds (7 cases) required immediate debridement, including amputation to prevent such unfavorable general infections, because aggressive local inflammatory reactions had already developed. Six of these patients had DM. Methicillin-resistant *Staphylococcus aureus* was isolated from almost all chronic wounds in patients with DM, which also suggested that HD-receiving patients with DM tend to bear multidrug-resistant organisms, and thus strict infection control is required to prevent outbreak.

CONCLUSION

Patients receiving HD because of DM were likely to have more severe and rapidly developing complex wounds because infections are common and because aggressive infections can be fatal. Thus, such patients usually require immediate debridement before blood access shunts become infected.

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IMMEDIATE RADICAL FANG MARK ABLATION MAY ALLOW TREATMENT OF JAPANESE VIPER BITE WITHOUT ANTIVENOM

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ABSTRACT: Administration of antivenom is currently the standard treatment for snake envenomation. However, it can sometimes cause anaphylactic reactions including urticaria, bronchospasm and hypotension. Furthermore, it may also provoke life-threatening complications, even though the mortality rate is less than 1%. In this study, we present a new treatment – immediate radical fang mark ablation – that was successfully performed on five victims of Japanese viper bites without antivenom use. In these five victims of venomous snakebites, surgical debridement was immediately performed. Two patients received a free-skin graft to resurface their wounds while three of them healed conservatively (i.e. by ointment treatment without surgery). After treatment, all patients could return to work. Immediate radical ablation is a recommended procedure that can reduce the amount of venom in tissues, which consequently decreases inflammatory reactions and reduces the necessity for antivenom.

KEY WORDS: ablation, viper bite, antivenom, fang mark, envenomation.

CONFLICTS OF INTEREST: There is no conflict.

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INTRODUCTION

More than 1,000 cases of Japanese viper (*Gloydius b. blomhoffii, Japanese mamushi*) bites are believed to occur annually in Japan (1). The venom of these snakes contains a chemically complex matrix of proteins that present enzymatic activities and cause local necrosis. On the other hand, this venom also contains low-molecular-weight polypeptides that increase capillary membrane permeability, resulting in plasma protein extravasations and red cell fragmentation. This lethal process can occur in many organs, including the lung, kidney, myocardium and central nervous system (2).

The most recent guidelines for first aid against viper envenomation call for avoiding the following measures: ice packs, incision, sucking, tourniquets and hot packs. The recommended therapy for a patient that presents rapid inflammation caused by viper envenomation is the administration of antivenom (3). However, it carries a risk of anaphylactic reaction, so that antivenom usage should be approached with extreme caution.

We successfully treated viper envenomation without antivenom by performing immediate radical fang mark ablation on five patients. This procedure is presented herein as a new first aid measure for victims of venomous snakebites.

CASE REPORTS

Case 1

A 72-year-old woman was bitten on her left leg by a Japanese viper and arrived at our unit 50 minutes after the injury. At initial examination, the medial side of the left knee was swollen with an area of ecchymosis and necrotic soft tissue measuring 3.5 x 2.0 cm around the fang mark (Figure 1). Surgical debridement of ecchymotic surface, as well as ischemic and necrotic tissue, including the surrounding inflamed skin (total of 8.5 x 7.0 cm) was immediately performed above the fascial layer under local anesthesia.

The wound was left open and wet-to-dry dressings were applied for five days. Severe systemic symptoms, including hypotension, respiratory distress or numbness were not observed, but the serum creatinine kinase (CK) level was remarkably increased (10,103 IU/L) throughout the subsequent week. The patient received tetanus toxoid (250 IU) and antibiotics (cefazolin, 2 g/day) intravenously as a prophylaxis against secondary infection. Antivenom was not administered due to the stable general

condition of the patient, which revealed constant renal function and normal platelet counts, prothrombin time and partial thromboplastin time. Two weeks later, the patient received a split-thickness skin graft to resurface the wound. Six months after the injury, the patient could return to work without any complications (Figure 2).

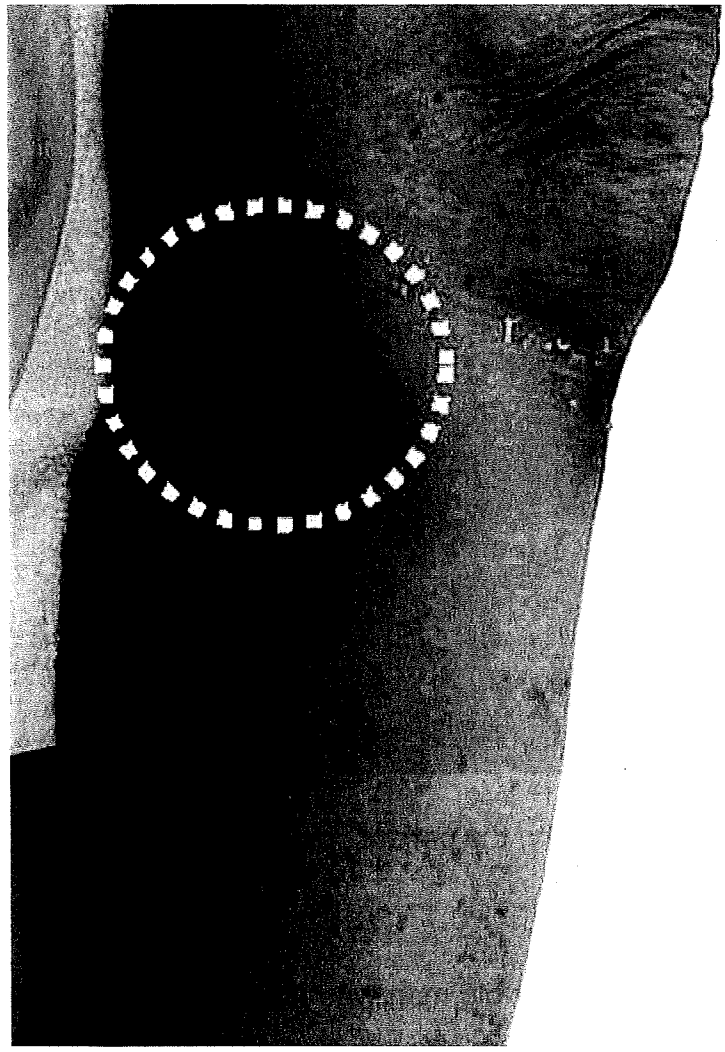

Figure 1. Initial examination showed that the left knee was swollen with an area of soft tissue necrosis measuring 3.5 x 2.0 cm around the fang mark. The dotted line indicates the debridement area.

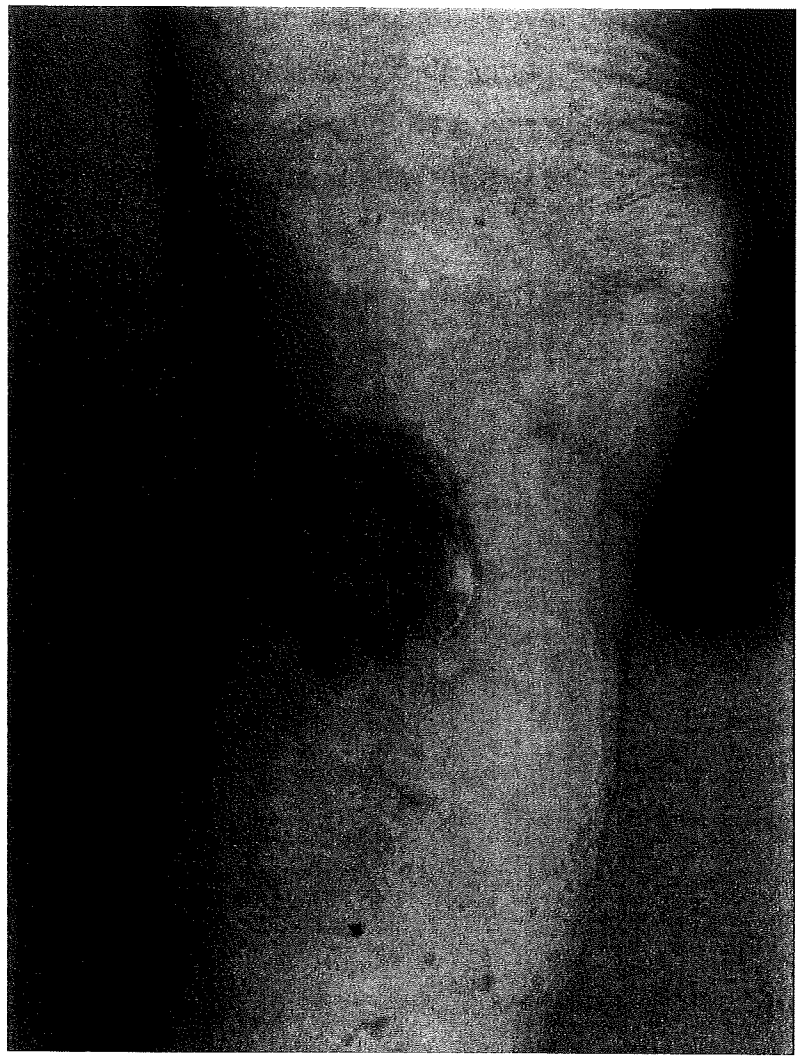

Figure 2. Six months after injury, the patient could return to work.

Case 2

The left index finger of a 74-year-old man was bitten by a Japanese viper. About 30 minutes after the injury, the victim arrived at our emergency unit where the first examination revealed that the radial side of the finger was swollen with an area of soft tissue necrosis measuring 1.5 x 0.6 cm around the fang mark (Figure 3). Immediate ablation was performed on the damaged skin, including the surrounding inflamed surface, covering a total area of 2.0 x 1.0 cm (Figure 4). The wound was left open for five days with wet-to-dry dressing. On the next day, severe systemic symptoms were not observed, but CK level was increased (1,248 IU/L). The patient received tetanus toxoid (250 IU) and antibiotics (cefazolin, 2 g/day) intravenously. Antivenom was not administered, since the general condition and laboratory data of

the patient indicated stability. Histopathological analysis of the fang mark site revealed red cell extravasation, fibrinoid necrosis of vessels and subcutaneous hemorrhagic necrosis (Figure 5). Treatment with ointment was performed, and the wound healed within two months with no sensory or functional impairment (Figure 6).

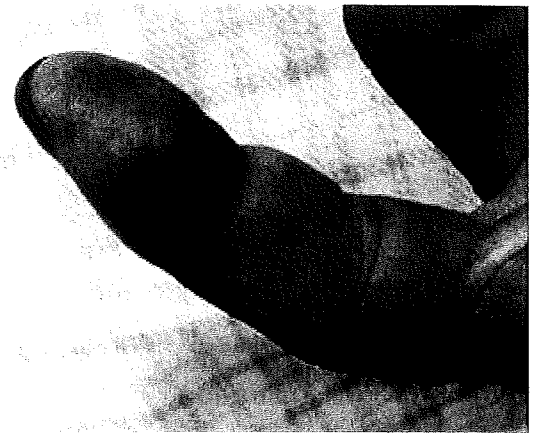

Figure 3. Examination about 40 minutes after injury revealed the swollen radial side of the left index finger with tissue necrosis area around the fang mark of 1.5 x 0.6 cm.

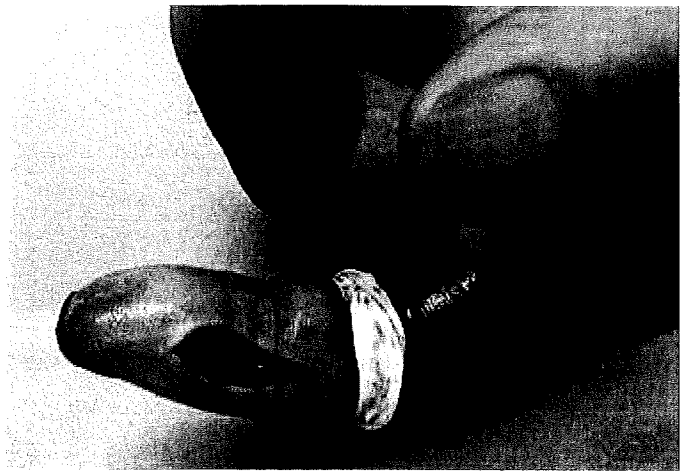

Figure 4. Wound appearance after removal of 2.0 x 1.0 cm area of soft tissue.

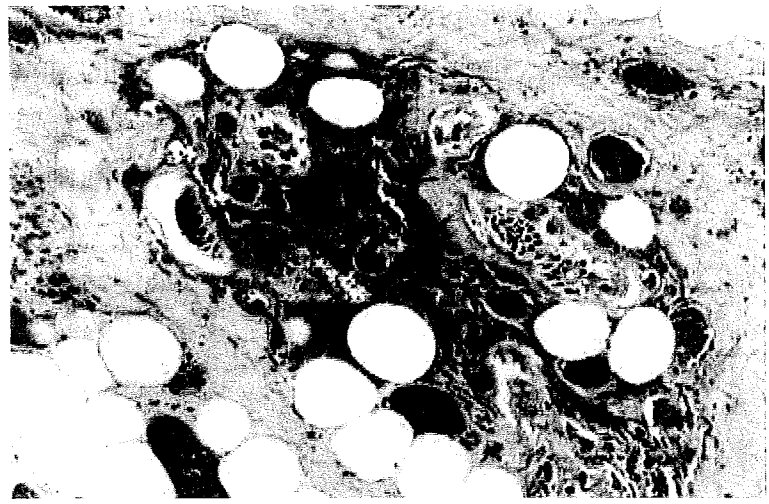

Figure 5. Histopathological findings of the fang mark site immediately after injury. Image shows red cell extravasation, vessel fibrinoid necrosis and subcutaneous hemorrhagic necrosis with neutrophil infiltration.

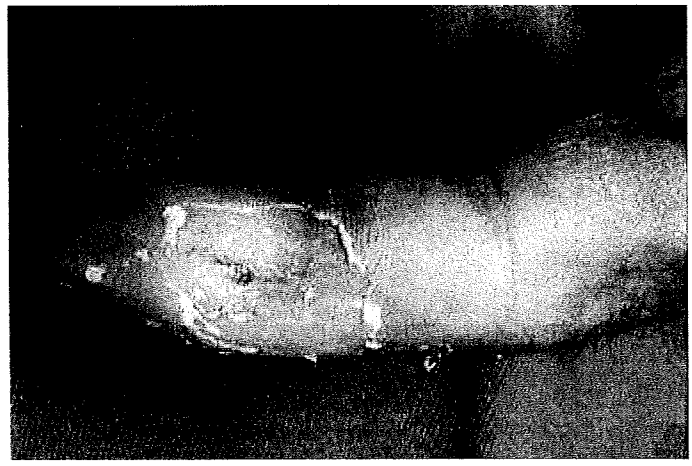

Figure 6. Two months after injury, the wound was completely healed.

Case 3

A 68-year-old woman was bitten by a Japanese viper on her left ring finger and was transferred to our emergency unit 30 minutes after the accident. The affected finger presented two lesions around fang marks characterized by swelling, ecchymotic area, ischemic soft tissue and measured, respectively, 1.0 x 0.8 cm and 0.6 x 0.5 cm (Figure 7). The necrotic tissue and inflamed skin areas were immediately ablated – 1.2 x 0.8 cm in each lesion (Figure 8). The wound was left open and conservative treatment with ointment was employed. Severe systemic symptoms were not observed, but the CK level was increased (11852 IU/L) for the following five days.

The patient received tetanus toxoid (250 IU) and antibiotics (cefazolin, 2 g/day) intravenously. Antivenom was not administered. The wound healed with slight numbness within 1.5 months (Figure 9).

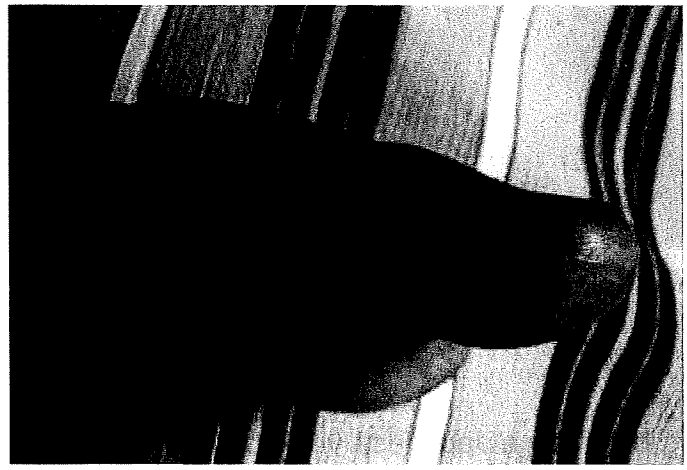

Figure 7. Two lesions on the left ring finger. Swelling and tissue necrosis are visible around fang marks (1.0 x 0.8 cm and 0.6 x 0.5 cm).

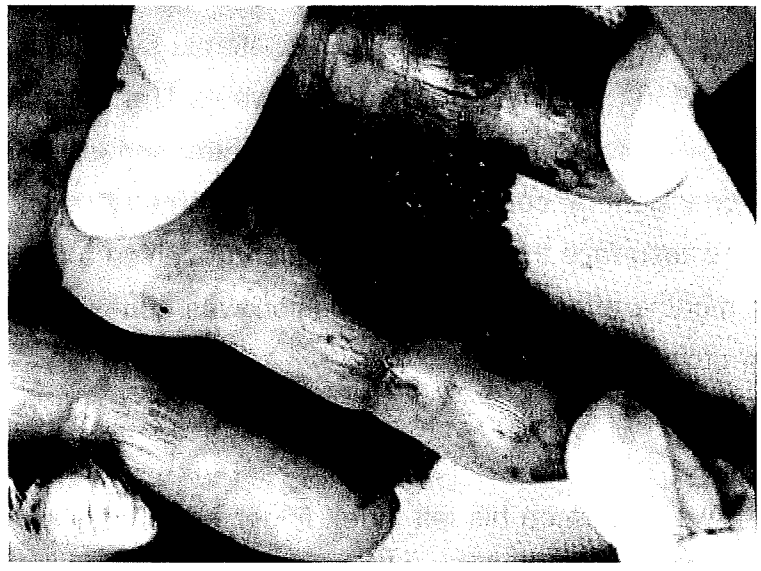

Figure 8. Necrotic soft tissue was immediately ablated.

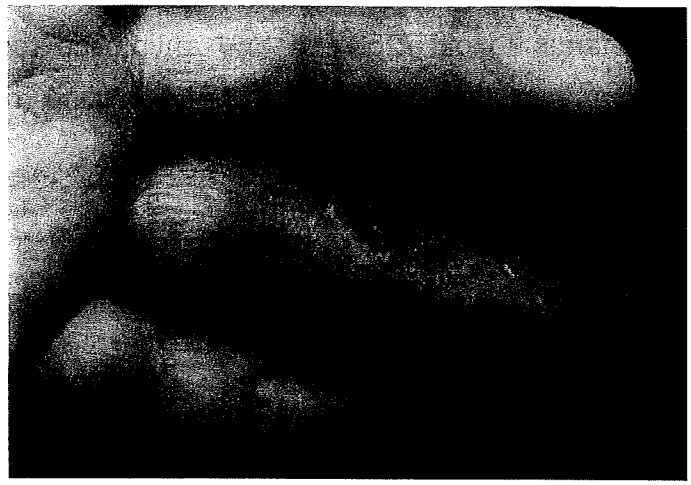

Figure 9. The wound healed with slight sensory disturbance within 1.5 months.

Case 4

One hour after being bitten by a Japanese viper on the right index finger, a 68-year-old man arrived at our emergency unit. First inspection revealed that the affected finger was swollen with soft-tissue necrosis surrounding the bite (0.8 x 0.5 cm). Immediate ablation of the damaged tissue was carried out, including the proximal inflamed skin (2.5 x 1.0 cm). The wound was left open and wet-to-dry dressing was applied for five days. The patient did not show systemic symptoms, except for the increased CK level (3988 IU/L) that persisted for a week. The victim received tetanus toxoid (250 IU) and antibiotics (cefazolin, 2 g/day) intravenously. Since the patient presented satisfactory general condition and stable laboratory tests, antivenom was not administered. To resurface the wound, the patient received a free skin graft three weeks later. Two months after the injury, the lesion was completely healed and the patient could return to work.

Case 5

A 78-year-old man was bitten on his left index finger by a Japanese viper and was transferred to our emergency unit one hour later. The finger was swollen with ecchymosis as well as ischemic soft tissue around the fang mark (0.3 x 0.2 cm). The necrotic tissue and inflamed skin were ablated (2.5 x 0.6 cm). The wound was left open and wet-to-dry dressings were applied. Besides a slight increase in the CK level (585 IU/L) for five days, systemic symptoms were not observed. The patient received tetanus toxoid (250 IU) and antibiotics (cefazolin, 2 g/day) intravenously, although antivenom was not administered. Conservative treatment with ointment was

performed, and the wound healed with no sensory or functional impairment within two months.

DISCUSSION

The venom of Japanese vipers contains a thrombin-like enzyme (1, 4). To treat viper envenomation, the first aid in the 1960s and 1970s included incision, sucking, stifling, and ice packs. However, in 1967, Russel (5) studied 147 patients who had received first aid and 78 who had not, and concluded that there was no evidence that the tratment had made any difference in short-term outcome. Kresanek *et al.* (6) also evaluated 58 cases of venomous snakebites and concluded that old types of first aid treatments were contradictories, since they can damage vessels and nerves, cause infections and worsen the wounds. For these reasons, old first aid methods are now strongly discouraged and the mainstay of hospital treatment for venomous snakebites is now administration of antivenom (3). Recent estimates suggest that the mortality rate is less than 1% for patients treated with the antivenom (1).

However, we believe there are some problems with the indiscriminate use of antivenom. The primary problems are anaphylaxis and serum sickness associated with antivenom treatment. Retrospective studies found that acute reactions, such as urticaria, bronchospasm and hypotension, occur in 23 to 56% of patients during the antivenom infusion (7). Punde (8) investigated 427 patients who received antivenom after envenomation by snakes, and reported that anaphylaxis due to anti-snake venom occurred in 11.7%. Furthermore, Biswas *et al.* (9) found unexpected severe complications of antivenom-induced myelopathy. Taking into account these studies, the use of antivenom should be prudent or avoided if possible.

Since snakebite severity depends on the amount of venom injected into the victim, if even a small part of it can be removed, patients should present milder symptoms (3). Measures to diminish venom volume into victims' body have been used since ancient times and include cutting and sucking as well as the use of suction devices. However, as previously stated, these first aid treatments are currently of no value and may actually worsen the bite wound (5, 6, 10).

Immediately after snakebite, envenomation occurs at the bite site causing swelling and skin necrosis around fang marks, which is also evident under histopathological examination (2, 9). Histopathological analysis of damaged tissue, including fibrinoid necrosis, vein thrombosis, red blood cell extravasation and subcutaneous tissue

necrosis, are consistent with the effects of the venom (2). Generally, injected venom diffuses proximally along the subcutaneous flow of lymph, inducing inflammatory reactions in the surrounding soft tissues.

We concluded that acute reactions – such as vascular obstruction and tissue necrosis – and necrotic changes were venom immediate effects, due to the observation of neutrophil infiltration. These types of reactions may be primarily local and delay their spread, so that a high dose of venom might remain close to fang marks for a long time. Therefore, the radical ablation of necrotic tissue and inflamed skin surrounding the bite would help reduce the amount of venom, which consequently decreases inflammatory responses and the necessity of antivenom.

In Case 1, the patient reported severe leg pain while swelling and necrotic tissue were visible on the knee. The bite probably had injected a large volume of venom, since the necrosis around fang marks developed rapidly. In our opinion, the immediate radical ablation of inflamed tissue was effective, even without administration of antivenom.

On the other hand, we have already seen victims of viper bites who had no symptoms or signs of envenomation several hours after injuries. In these dry-bite cases, radical ablation of fang mark should not be performed until local signs of envenomation appear, i.e., ecchymosis, ischemia, swelling, increasing pain and skin necrosis.

Since the aim of this procedure is removal of injected venom, all necrotic soft tissue and inflamed skin must be debrided. The earlier the treatment is performed, the smaller is the area that must be removed. Our five cases suggested that effective venom removal can be expected if ablation is carried out within an hour after bite. Regrettably, if a large soft-tissue defect results from ablation, a surgical resurfacing procedure – like skin graft or local flap transfer – is required, as occurred in Cases 1 and 4.

Although immediate radical ablation can reduce the volume of injected venom, a total removal is impossible. Continuous observation is indispensable after ablation, and if severe systemic symptoms of envenomation occur – including shock intensification, severe local swelling, digestive or neurological symptoms, and continuous clotting abnormalities – antivenom treatment should be indicated with no hesitation.

Immediate radical ablation is a useful procedure that can reduce the amount of venom in tissue, which, consequently, decreases inflammatory reactions and reduces the necessity of antivenom usage.

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WOUNDS
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Evaluation of Nutrition in the Healing of Pressure Ulcers: Are the EPUAP Nutritional Guidelines Sufficient To Heal Wounds?

Takahiro Yamamoto, Masaki Fujioka, MD, PhD, Riko Kitamura, MD, Aya Yakabe, MD, Hironori Kimura, MD, Yoshinori Katagiri, Hiroyo Nagatomo

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Evaluation of Nutrition in the Healing of Pressure Ulcers: Are the EPUAP Nutritional Guidelines Sufficient To Heal Wounds?

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Abstract: Malnutrition is a significant factor in the development of pressure ulcers and many nutritional guidelines for preventing pressure ulcers have been published. However, few clinical investigations have examined the energy required to heal pressure ulcers. The aim of the present study was to investigate the relationship between nutritional intake and improvement of pressure ulcers. Total calories, which were supplied by mouth through a feeding tube and via venous alimentation were examined for 40 hospitalized bedridden inpatients who had pressure ulcers. Of these patients, 21 whose wounds improved or healed and 19 whose wounds became worse or did not improve were eligible for this retrospective study. Pressure ulcers in patients who received more than 30 kcal/kg per day improved or healed, while those of patients who received less than 20 kcal/kg per day worsened or failed to improve. Furthermore, intake of 30 kcal/kg per day enabled serum albumin levels to improve. Energy intake of 30 kcal/kg per day is comparable to the predicted total energy expenditure and is thought to be essential for improving pressure ulcers in bedridden patients.

Malnutrition is a significant factor in the development of pressure ulcers and many studies have shown that early nutritional assessment is essential for preventing pressure ulcers.[1] Many nutritional guidelines for preventing pressure ulcers have been published because ulcers tend to develop in patients with malnutrition despite intensive care.[1] However, few reports have recommended levels of energy intake needed to heal pressure ulcers. The present study investigated the total nutritional intake of patients with pressure ulcers to determine the level of energy intake needed to heal pressure ulcers.

Methods

Forty patients with pressure ulcers at Nagasaki Medical Center (Nagasaki, Japan) were treated from August 2007 through February 2008. Of these patients, 21 whose wounds improved or healed (improvement group) and

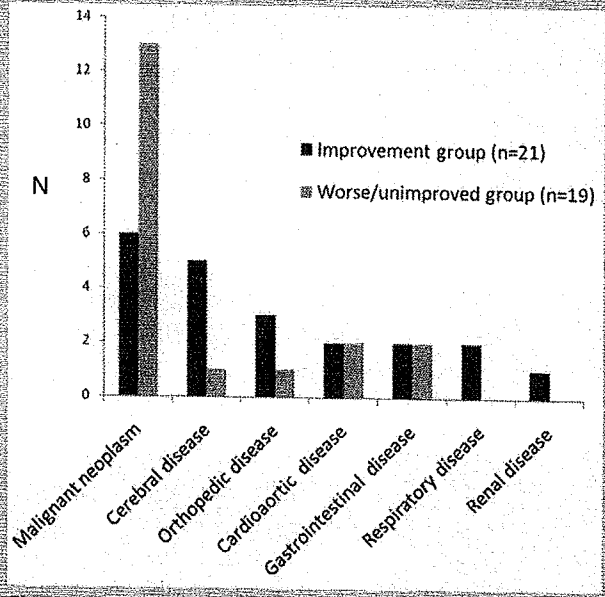

Figure 1. Primary diseases in patients.

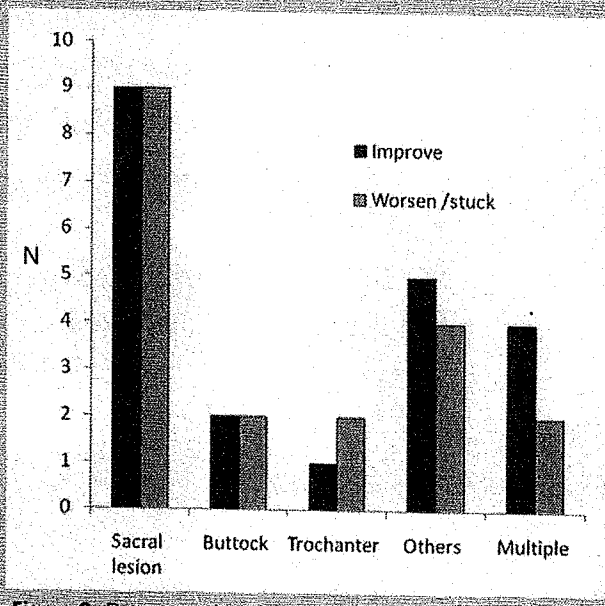

Figure 2. Pressure ulcer locations.

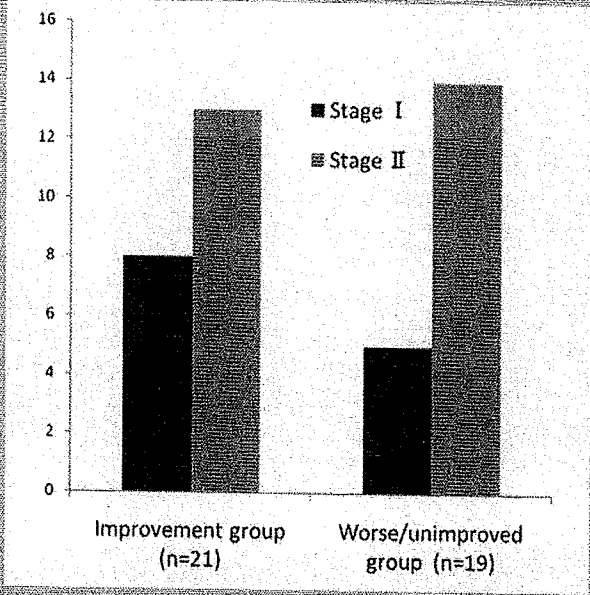

Figure 3. Initial pressure ulcer stages.

19 whose wounds became worse or did not improve (worse/unimproved group) were eligible for this retrospective study. Primary diseases are shown in Figure 1. In both groups, malignant neoplasms were the most common primary disease.

Patients in the improvement group ranged in age from 22 to 94 years (mean age, 67.4 ± 16.4 years), and patients in worse/unimproved group ranged in age from 51 to 92 years (mean age, 71.7 ± 10.9 years). Pressure ulcer locations are shown in Figure 2. Pressure ulcers developing over the sacrum accounted for about half of all ulcers in both groups. The severity of the pressure ulcers at discovery is shown in Figure 3. The severity of the pressure ulcers was similar in both groups, in that only Stage I and Stage II ulcers were discovered; this finding indicates that these pressure ulcers were discovered within the early stage.[2] Eight of 21 patients (38%) in the improvement group and 5 of 19 (26%) presented with a Stage I pressure ulcer. Differences in wound severity may account for bias in the study. However, changes in the wounds were investigated (improvement or worsening), and it was assumed that the influence of the primary wound state had little effect on the reported results. Regardless of stage, pressure ulcers usually will improve when they are treated with proper wound bed preparation, use of extra-soft mattresses, and proper alimentation.[1,3,4] All patients in this study underwent desirable wound treatment and were placed on either a low-air loss mattress or an extra-soft mattress. Despite these curative efforts, worsened or unimproved pressure ulcers were still seen mainly as a result of insufficient nutritional support.

Height, body weight, body mass index (BMI), and serum albumin level before the pressure ulcer developed in patients in the improvement group and in the worse/unimproved group are shown in Table 1. There were no significant differences in these variables between the improvement group and the worse/unimproved group.

Table 1. Age, height, body weight, BMI, and serum albumin of patients with pressure ulcers.

	Age (years)	Height (cm)	Body weight (kg)	BMI (kg/m²)	Serum albumin (g/dl)
Improvement (n = 21)	67.4 ± 16.4	155.8 ± 9.7	45.7 ± 10.3	18.7 ± 3.3	2.8 ± 0.6
Worse/unimproved (n = 19)	71.7 ± 10.9	157.8 ± 12.5	48.1 ± 8.9	19.9 ± 3.2	3.0 ± 0.9

To evaluate ulcer changes, all patients were observed each week at least 1 month from the time the pressure ulcer was discovered. Patients who were discharged before the pressure ulcer healed and either died at home or in hospice within 1 month were excluded from the study. The size, depth, increase in granulation, amount of exudate and necrotic tissue, and development of wound infection were recorded each week. Then, each wound was judged to be either in the healing phase, worsening phase, or the unimproved phase. During the study, all wounds were treated with the usual methods of wound bed preparation including debridement, exudate management, bacterial imbalance resolution, and moist wound dressings; low-air loss mattresses or extra-soft mattresses were supplied to all patients.[3] The total daily energy intake, including that through normal feeding, oral supplementation, tube-feeding, and intravenous alimentation were determined and investigated. The nutritional intake was measured on the day the pressure ulcer was discovered and 2 weeks before and 2 and 4 weeks after discovery.

We investigated several problems when patients developed pressure ulcers including: 1) whether wound healing is affected by total energy intake, and 2) if so, how many calories are required for wound healing? Statistical analysis was performed using Student's t-tests.

Ethical considerations. The study's procedures were in accordance with the ethical standards of the Nagasaki Medical Center's institutional committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 1983.

Results

Changes in total energy intake in patients of both groups are shown in Figure 4. The mean total energy intake per kilogram of body weight in the improvement group was higher than that in the worse/unimproved group. Total energy intake in the improvement group was always greater than 30 kcal/kg body weight (kcal/kg), whereas in the worse/unimproved group, energy intake was not greater than 20 kcal/kg throughout the observation period. There was a significant difference between the groups in total energy intake at each time point during the 6 weeks ($P < 0.01$).

Changes in daily protein intake for patients in both groups are shown in Figure 5. The mean daily protein intake in the improvement group was higher than that in the worse/unimproved group. Protein intake in the improvement group was always greater than 45 g, whereas that in the worse/unimproved group was about 20 g

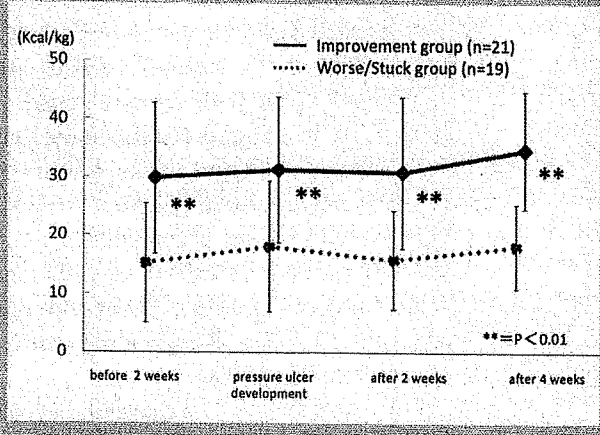

Figure 4. Changes in total daily energy intake.

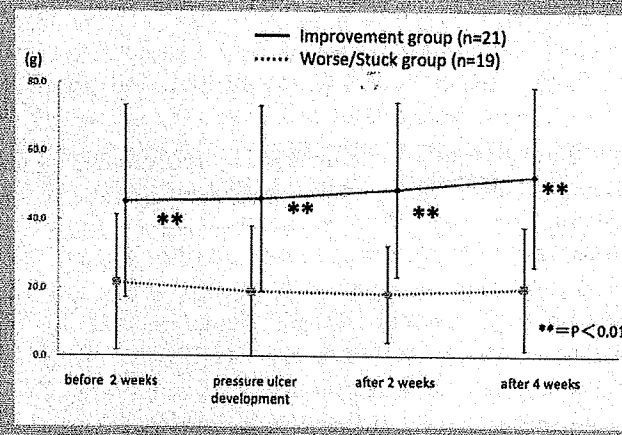

Figure 5. Changes in total daily protein intake.

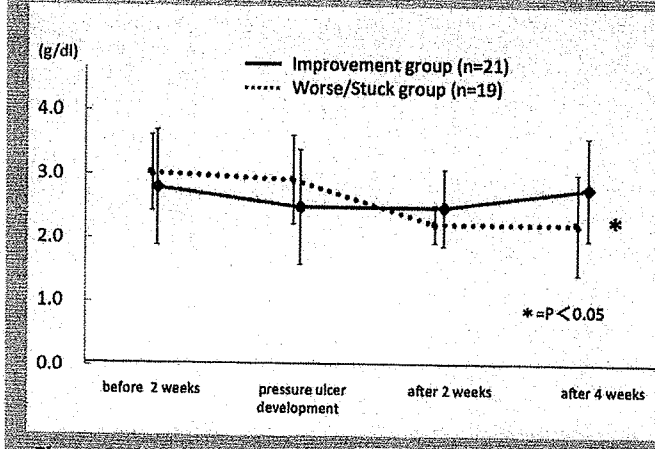

Figure 6. Changes in serum albumin.

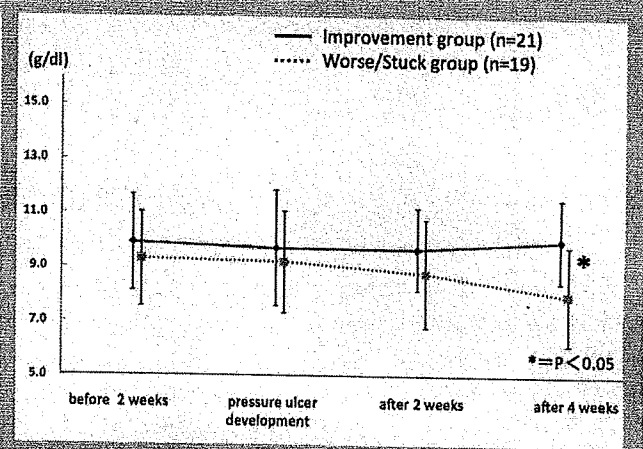

Figure 7. Changes in hemoglobin.

throughout the observation period. There was a significant difference between the groups in daily protein intake at each time point during the 6 weeks ($P < 0.01$).

Changes in serum albumin levels are shown in Figure 6. Mean serum albumin levels of the worse/unimproved group decreased throughout the observation period, whereas those in the improvement group increased after pressure ulcers developed. The mean serum albumin levels in the improvement group was significantly higher than that in the worse/unimproved group 4 weeks after the wound developed ($P < 0.05$), although the initial serum albumin level in the improvement group was lower than that in the worse/unimproved group. Changes in hemoglobin levels are shown in Figure 7. Mean hemoglobin levels of the worse/unimproved group decreased throughout the observation period, whereas those in the improvement group were almost stable at 10 g/dL.

Discussion

Pressure ulcers and malnutrition have a strong correlation.[1] Many clinical studies of malnutrition and pressure ulcers have been performed. These studies have shown that a relevancy of an increase in pressure ulcers and the presence of malnutrition or a decreased intake of energy are related.[5-7] The European Pressure Ulcer Advisory Panel (EPUAP) issued clinical nutritional guidelines for preventing pressure ulcers in 2004, which recommended that a patient requires a minimum of 30 kcal/kg to 35 kcal/kg per day to prevent pressure ulcer development. All of the patients in the present study had a BMI of 18.5 kg/m^2 to 20 kg/m^2, indicating they were underweight or chronically malnourished (Table 1). The EPUAP nutritional guidelines also suggest that a similar strategy of nutritional intervention should be considered for the treatment of patients who have established pressure ulcers.[8] However, few reports have indicated recommended intake levels to heal pressure ulcers.

An insufficient dietary intake impairs wound healing, because a poor nutritional status decreases collagen synthesis, skin elasticity, antibiotic levels, general cellular turnover, and the ability to fight infection.[8] Accordingly, the EPUAP nutritional guidelines recommend that patients with pressure ulcers require 30 to 35 kcal/kg for wounds to heal.[7] The results of the present study show that the total energy intake in patients whose pressure ulcers improved was greater than 30 kcal/kg per day, whereas energy intake in patients whose ulcers worsened or did not improve was not more than 20 kcal/kg per day. These results were unexpected, because we believed that extra calories were required to heal pressure ulcers. The EPUAP nutritional guidelines were intended mainly to prevent pressure ulcers from developing, meaning that some of the targeted patients are ambulatory. Conversely, all of the patients in the present study were bedridden and had energy requirements that were thought to be lower than those of nonbedridden patients.[10] Energy intake of 30 kcal/kg per day is comparable to the predicted total energy expenditure (1.2 × basal energy expenditure) and is thought to be sufficient for bedridden patients. As proof, intake of 30 kcal/kg per day facilitates an increase in serum albumin levels, which would also encourage wound healing.

The present study revealed that the mean energy intake in the worse/improved group was less than 20 kcal/kg per day, which suggests that wounds cannot be

expected to improve in patients whose energy intake is 20 kcal/kg or less per day. This result indicates that improving wounds is almost impossible in patients whose feeding is interrupted because of some disorder of digestion or absorption including nausea, vomiting, unpleasantness of tube placement, and repeated pneumonia caused by bronchial reflex despite tube feeding. These unpleasant disturbances are likely to occur in patients with malignant neoplasms especially in the terminal stage.[11] This notion is supported by the primary disease being a malignant neoplasm in 13 of 19 patients (68%) whose pressure ulcers did not improve, but in only 6 of 21 patients (26%) whose pressure ulcers did improve.

Nutritional support with more than 30 kcal/kg per day for patients with pressure ulcers should encourage wound healing and increase serum albumin levels.

Conclusion

The use of nutritional guidelines in pressure ulcer care has been recommended since malnutrition is a significant factor in both the development and healing of pressure ulcers. However, these guidelines were mainly intended to prevent formation of pressure ulcers. To encourage wound healing, total energy intake of 30 kcal/kg per day is essential for bedridden patients with pressure ulcers.

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Combination Treatment with Basic Fibroblast Growth Factor and Artificial Dermis Improves Complex Wounds in Patients with a History of Long-Term Systemic Corticosteroid Use

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Wound bed preparation has allowed uncomplicated wounds to heal quickly without surgery, but the treatment of some complex chronic wounds remains challenging.[1] Wounds induced by collagen disease are particularly hard to heal because patients are usually treated with steroids for a long period.[2,3]

Treatment with angiogenic cytokines allows these chronic ulcers to heal more quickly.[4,5] In addition, artificial dermis is beneficial for the reconstruction of wounds with exposed tendons or bone.[6] We report the outcomes of chronic ulcers caused by collagen disease and collagen vascular disease in four patients who had been treated with high-dose steroids and underwent combination treatment with basic fibroblast growth factor (bFGF) and artificial dermis.

Patients and Methods

One hundred ninety-one patients with chronic ulcers were treated in the Department of Plastic and Reconstructive Surgery, National Organization Nagasaki Medical Center, in 2005 and 2006. Four of these patients who had complex ulcers due to collagen disease and collagen vascular disease and had been treated with steroids underwent combination treatment (Table 1). Ulcers in these four patients had not healed with conventional treatment including surgical debridement, ointment therapy, and free skin grafting.

The artificial dermis is composed of two layers: a lower layer of atelocollagen and an upper layer of silicone. The atelocollagen was purified from porcine-tendon collagen, neutralized, and freeze-dried to make sponge membranes (Pelnac, Gunze Co. Ltd., Kyoto, Japan). The artificial dermis was cut with multiple slits, like a mesh skin graft, through which exudates can be drained and sprayed bFGF can reach the atelocollagen sponge.

After debridement, the slit artificial dermis was applied to the wounds, and bFGF (trafermin, Fiblast Spray, Kaken Pharmaceutical Co. Ltd., Tokyo, Japan) was sprayed (Figure 1). Ointment-impregnated gauze was applied to the wounds. Treatment with bFGF continued until patients underwent secondary skin grafting.

Cases

Case 1: A 30-year-old woman with systemic lupus erythematosus (SLE) who had been treated with 20 mg per day of prednisolone for 8 years had a necrotic ulcer on the right buttock. After debridement, cleansing and wet-to-dry dressing was continued for 1 month, but a favorable wound bed did not develop (Figure 2A). Debridement was performed again, and an artificial dermis was applied, after which bFGF was sprayed every day (combination treatment). After 1 month, abundant granulation tissue had developed on the wound surface (Figure 2B). The patient underwent free skin grafting. The wound was completely resurfaced by 1 month after skin grafting, and has been maintained without relapse for 3 years (Figure 2C).

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