Case Report

Two Refractory Cases of Ulcer with Achilles Tendon Exposure Treated with bFGF Inserted into Pelnac-Gplus® Following Negative Pressure Wound Therapy

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ABSTRACT

Skin leg ulcers with Achilles tendon exposure are refractory to conventional treatments. These ulcers are caused by conditions such as diabetes, venous insufficiency, arterial sclerosis, and collagen disease. We encountered two cases of refractory skin leg ulcers with Achilles tendon exposure. These patients have venous insufficiency and take a long time to cure at other hospitals. We used an artificial dermis, namely Pelnac-Gplus®, combined with a basic fibroblast growth factor (bFGF) formulation to treat these ulcers following negative pressure wound therapy for a month. A good result was obtained two weeks after the skin graft was performed. One year postoperatively, the lesion was followed a good course, and the ulcers did not recur.

Key words: Achilles tendon, artificial dermis, basic fibroblast growth factor (bFGF), chronic ulcer, negative pressure wound therapy (NPWT), Pelnac-Gplus®

Introduction

Skin ulcers on the lower leg can be caused by diabetes, venous insufficiency, pressure sores, collagen disease, trauma, or radiation. These ulcers might become refractory with conservative treatment, especially in cases of Achilles tendon exposure. Additionally, ulcers on the posterior of the lower leg are difficult to close simply or to the local flap; invasive surgeries such as free flaps are required in some cases. However, many of these patients have several conditions, such as arterial sclerosis, diabetes, venous insufficiency, or collagen disease. Many patients want non-invasive treatment and early rehabilitation and to return to their daily lives earlier.  

We report two cases of refractory leg ulcer with Achilles tendon exposure caused by venous insufficiency treated using an artificial dermis, Pelnac-Gplus® (Gunze Corp., Osaka, Japan) containing basic fibroblast growth factor (bFGF) preparation (FIBRAST SPRAY®; Kaken Pharmaceutical, Tokyo, Japan). Two ulcers formed good granulation tissue with Pelnac-Gplus® and bFGF, and skin grafting was performed two weeks later with good results.

In 2018, Pelnac-Gplus® was newly developed from Pelnac® (Gunze Corp., Osaka, Japan). Pelnac-Gplus® contains 10 wt% acidic gelatin, which can sustain the release of positively charged growth factors, such as bFGF. Combining Pelnac-Gplus® with bFGF accelerated neovascularization and the formation of dermis-like tissue earlier than when a conventional artificial dermis is used.

Treating leg ulcers with Pelnac-Gplus® with bFGF has been proven minimally invasive and effective in a short period, especially in cases with exposed tendons or bones.

Case report

Case 1: A 78-year-old woman had been diagnosed with chronic anemia and Sjögren’s syndrome with systemic lupus erythematosus (SLE) about twenty years prior and was taking oral steroids (prednisolone, 5 mg). The ulcer developed on her left lower leg, after which
cellulitis formed around the wound. A dermatologist performed the debridement. When the patient visited our outpatient clinic, redness and dermal pockets were observed around the ulcer, along with Achilles tendon exposure. We began to spray the bFGF formulation on the wound and performed negative pressure wound therapy (NPWT) twice a week for a month. The skin pocket, redness around wound and other infection signs disappeared, so we performed debridement and placed Pelnac-Gplus® containing bFGF (FIBRAST SPRAY®) on the ulcer. When the silicone sheet of Pelnac-Gplus® was removed one week after this procedure, good granulation was observed. After another week, split-thickness skin grafts from the lower abdominal wall were applied. The skin graft survived well (Fig. 1a–e).

Case 2: A 57-year-old man presented with an ulcer on his left lower leg. In several orthopedic clinics, he received conservative treatment such as ointment, and he underwent high ligation vascular surgery with a diagnosis of varicose veins of the lower extremities. However, the ulcer did not improve. Subsequently, an Achilles tendon rupture was discovered, and he underwent necrotic tendon resection and tendon reconstruction with a transfer from the gastrocnemius muscle at an orthopedic clinic. However, the reconstructed tendon was infected and exposed, and Staphylococcus aureus was detected in the wound. When he visited our outpatient clinic, necrotic tendon-like tissue, bad granulation, and a dermal pocket around the ulcer were observed. Infection was also found. We performed NPWT and applied bFGF (FIBRAST SPRAY®) twice a week for a month. Although good granulation was observed on the ulcer, the tendon was still exposed. We then performed debridement and placed the Pelnac-Gplus®, which contained bFGF. One week after this procedure, we removed the silicone sheet of Pelnac-Gplus® and confirmed that the transferred muscle was covered with good granulation tissue; however, a small area of tendon was still exposed. After another week, split-thickness skin grafts were performed from the lower abdominal wall. The skin graft survived well (Fig. 2a–e).

Discussion

Pelnac® (Gunze Corp., Osaka, Japan) was first reported in Japan by Suzuki et al15 and is constructed in two layers, including an atelocollagen sponge layer and silicone membrane. Pelnac®, like any other artificial dermis, has been used to treat full-thickness skin defects caused by burns, trauma, tumor resection, etc. After the artificial dermis is applied to skin defects, fibroblasts and capillaries penetrate and proliferate in the collagen sponge, and dermis-like tissue is formed after the collagen sponge is degraded15-17. However, it is difficult to use an ordinary artificial dermis for chronic skin ulcers as infection can occur easily. This is because the capillaries are susceptible to infection before they infiltrate the inner collagen sponge18. Pelnac-Gplus® was newly developed in 2018, and contained 10 wt% acidic gelatin. It bonds positively charged growth factors, such as bFGF, and can sustain release for longer than 10 days6 (Fig. 3a, b). Several studies using mice and beagle dogs have shown that Pelnac-Gplus® itself can be used as a scaffold for dermal regeneration, similar to conventional Pelnac®. Pelnac-Gplus® with bFGF accelerates neovascularization and the formation of dermis-like tissue two or three times faster than that attained using conventional Pelnac® 7-10. Accelerated vascularization can eliminate the artificial dermis’ weakness of being vulnerable to infection.

bFGF, which was identified in 1974, promotes the proliferation of fibroblasts and capillary formation and...
accelerates tissue regeneration\textsuperscript{14,19}. Human recombinant bFGF has been used clinically to treat chronic skin ulcers, burns, and skin defects, and its clinical effectiveness has been demonstrated\textsuperscript{20}. bFGF has the ability not only to promote fibroblast proliferation, but also strong angiogenesis in artificial dermis\textsuperscript{21,22}. This results in the early formation of dermis-like tissue and promotion of wound healing.

In the present two cases, the patients had already been undergoing treatment for a long time, so they sought early resolution. In the first case, the patient had collagen disease, venous insufficiency, and old age and should not have been treated invasively. In our two cases these ulcers soon showed healthy granulation after treatment bFGF inserted into Pelnac-Gplus\textsuperscript{®} despite tendon exposure, similar to the case in the clinical trial report of Pelnac-Gplus\textsuperscript{®} with bFGF\textsuperscript{13}.

It was suggested that the main reason for the early healing of these cases was the strong angiogenic effect of bFGF on vascular endothelial cells in addition to the fibroblast proliferation effect of bFGF. Pelnac-Gplus\textsuperscript{®} contains gelatin that ionically binds with bFGF and releases it slowly and continuously on the wound, and these effects of bFGF continue to affect these multiple cells in the wound.

We often encounter refractory ulcers with tendon or bone exposure and artificial objects such as irremovable artificial blood vessels and metal devices. It is very difficult to heal these ulcers and infections occur around these tissues in these cases. Therefore, it is important to control the infection. Therefore, we considered that after the infection had subsided following NPWT, treatment with Pelnac-Gplus\textsuperscript{®} containing bFGF proved extremely useful.

**Conclusion**

Leg ulcers with tendon exposure are difficult to treat. In the
two cases described in the present report, treatment using Pelnac-Gplus® containing a bFGF preparation was very useful.

The novel Pelnac-Gplus® contains gelatin that bonds ionically with bFGF, maximizing its effects and exerting a tremendous effect on refractory ulcers with exposed tendons and bones.

Conflicts of interest

There are no conflicts of interest to declare.

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