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CASE REPORT

# Non-surgical treatment of diabetic foot ulcers on the dorsum of the foot with polydeoxyribonucleotide injection: Two case reports

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## Abstract

*BACKGROUND*

Diabetic foot ulcers are caused by a variety of factors, including peripheral neuropathy, peripheral arterial disease, impaired wound healing mechanisms, and repetitive trauma. Patients with diabetic foot ulcer on the dorsum of the foot are often treated surgically. However, the right non-surgical therapy must be chosen if surgical choices are contraindicated or if the patient prefers conservative treatment over surgery.

*CASE SUMMARY*

The purpose of this case report is to highlight the efficacy of polydeoxyribonucleotide (PDRN) injection as a non-surgical treatment option for diabetic foot ulcers on the dorsum of the foot, particularly in patients who choose against surgical intervention. This case report presents two cases of diabetic foot ulcers located on the dorsum of the foot that were successfully treated with PDRN injection as a non-surgical intervention.

*CONCLUSION*

If the patient declines surgery for diabetic ulcers with Wagner grade II or below, PDRN injection can be effective if necrotic tissue is removed and the wound bed kept clean.

**Key Words:** Diabetic foot; Wound healing; Regenerative medicine; Polydeoxyribonucleotides; Case report

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**Core Tip:** If a diabetic foot wound of Wager grade II or less is located on the dorsum of the foot and is not amenable to surgical treatment, polydeoxyribonucleotide injection combined with a minimally invasive treatment of debridement under local anesthesia may help wound healing in patients who are not amenable to surgical treatment.

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## INTRODUCTION

Diabetic foot ulcers are caused by a variety of factors, including peripheral neuropathy, peripheral arterial disease, impaired wound healing mechanisms, and repetitive trauma, and are a fatal condition that affects 19%-35% of people with diabetes mellitus and can lead to amputation and death[1]. Proper care of diabetic foot ulcers is an important factor to increase patient outcome and favorable prognosis[2]. Patients with diabetic foot ulcer on the dorsum of the foot have often been treated surgically using techniques like free flap[3] or local flaps[4]. However, the right non-surgical therapy must be chosen if surgical choices are contraindicated or if the patient prefers conservative treatment over surgery.

It is important to choose an effective non-surgical treatment option if the patient declines surgical reconstruction because foot ulcers in the midfoot heal more slowly and require longer than ulcers in the toe[5]. Additionally, if possible, amputation should be performed distally[6], but ulcers in the dorsum of the foot may require a more proximal amputation than the toe.

Free flap surgery, also known as free tissue transfer, involves transferring tissue with its blood supply from one part of the body to another for reconstructive purposes. The procedure allows for the repair of diabetic foot ulcers by using healthy tissue from elsewhere in the body. Through microsurgery techniques, the transferred tissue is reconnected to blood vessels at the recipient site. Free flap is the preferred surgical treatment for diabetic foot ulcers with good prognosis and increased survival rate[7]. However, free flap reconstruction requires careful surgical planning, a long stay in the hospital, and can be accompanied by potential surgical complications[8] such as flap failure, donor site morbidity, infection, or wound dehiscence, as well as a shallow learning curve for the surgeon to become proficient in microsurgery.

A substance generated from salmon DNA called PDRN has shown extraordinary abilities in the processes of tissue regeneration, wound healing, and anti-inflammatory responses. Many *in vitro* studies[9,10], animal studies[11,12], and clinical studies[13] have demonstrated its effectiveness, and it is expanding its scope by demonstrating its effectiveness in the reconstructive field.

The purpose of this case report is to highlight the efficacy of PDRN injection as a non-surgical treatment option for diabetic foot ulcers on the dorsum of the foot, particularly in patients who choose against surgical intervention. This case report presents two cases of diabetic foot ulcers located on the dorsum of the foot, successfully treated with PDRN injection as a non-surgical intervention. Both cases involved patients with longstanding diabetes and chronic non-healing ulcers, warranting alternative therapeutic options due to the risks associated with surgical procedures and the limited response to conventional wound care measures.

## CASE PRESENTATION

### *Chief complaints*

**Case 1:** A 68-year-old man who had a soft tissue defect to the left dorsum of his foot (Wagner grade II) measuring about 3 cm  3 cm and present for 6 mo came to the plastic surgery outpatient department (Figure 1).

**Case 2:** A 70-year-old woman who had a soft tissue defect to the right dorsum of her foot (Wagner grade II) measuring about 2 cm  2.5 cm and present for 3 mo came to the plastic surgery outpatient department (Figure 2).

### *History of present illness*

**Case 1:** The patient received conservative care with regular dressings, but the wound condition did not improve.

**Case 2:** The patient first had a small wound that another hospital tried to stitch closed. However, her wound did not heal, and she eventually came to the plastic surgery outpatient department with wet eschar and significant necrosis.

### *Personal and family history*

**Case 1:** This patient did not have a family history of diabetic foot ulcers.

**Case 2:** This patient did not have a family history of diabetic foot ulcers.



**Figure 1 Case 1, pretreatment photograph after initial debridement.** The diabetic foot ulcer measuring 3 cm  3 cm on the dorsum of the left foot with exposure of muscle and tendon (Wagner grade II).




**Figure 2 Case 2, pretreatment photograph before and after initial debridement.** The diabetic foot ulcer measuring 2 cm  2.5 cm on the dorsum of the right foot with exposure of muscle (Wagner grade II). A: Pretreatment photograph before initial debridement; B: Pretreatment photograph after initial debridement.

### *Physical examination*
**Case 1:** His ankle-brachial index (ABI) was 0.96.

**Case 2:** Her ABI was 0.91.

### *Laboratory examinations*
**Case 1:** His HbA1c was 9.6%, indicating poor blood sugar control.

**Case 2:** Her HbA1c was 8.8%, suggesting poor blood sugar control.

### *Imaging examinations*
No additional radiologic study was performed.

## FINAL DIAGNOSIS
Hard-to-heal Diabetic foot ulcers.

## TREATMENT

**Case 1:** We first advised surgery, such as a free flap, but the patient declined because of anxiety over potential complications. In consideration of this, we began conservative treatment with PDRN and adequate glycemic control. PDRN (5.625 mg) was intralesionally injected into the subcutaneous layer of the wound once a week for a total of 8 wk after we debrided the necrotic tissue of the wound at the patient's initial visit. The patient applied a wet-to-dry gauze dressing to the wound daily while receiving therapy.

**Case 2:** As in case 1, we first recommended surgery, but the patient refused. PDRN (5.625 mg) was injected in a perilesional manner into the subcutaneous layer once a week after the necrotic tissues had been surgically debrided, and daily wet-to-dry gauze dressing was applied as in case 1.

## OUTCOME AND FOLLOW-UP

**Case 1:** After about 2 wk of dressing and two PDRN treatments, there was no noticeable healing effect, so we debrided the unhealthy tendon (extensor digitorum brevis) that was exposed during the dressing, and the wound began to show noticeable wound healing.

Eight weeks later, the patient's diabetic foot ulcer had epithelialized and had fully recovered without any sequelae (Figure 3). He recovered from his diabetic foot ulcer, and it did not get worse over the following 2 mo.

**Case 2:** After 8 wk, the diabetic foot ulcer on the dorsum of her foot had healed and left no significant sequelae (Figure 4). There were no complications at the 1-mo follow-up.

## DISCUSSION

If surgical repair for a diabetic foot ulcer on the dorsum of the foot is available, it is the usual treatment choice. However, there are few conservative treatment options available for the patients who choose to refuse surgical procedures. Collagen dressing[14], acellular fish skin dressing[15], negative-pressure wound therapy[16], and other treatments are known to aid in the healing of diabetic foot ulcers, but their broad usage is limited due to the high cost and difficulties in carrying the device. However, PDRN had a positive effect on wound healing in these cases with just one weekly injection and without the disadvantages described above. Therefore, it can be another treatment option for patients who refuse surgical treatment.

The observed healing response in the dorsum of the foot following PDRN injections supports prior studies[9-12] that demonstrated PDRN's therapeutic potential in stimulating tissue regeneration. PDRN's angiogenic features are thought to play a critical role in encouraging blood vessel creation and increasing local microcirculation, resulting in improved wound healing.

In diabetic foot ulcer patients with severe vascular compromise, revascularization is a critical intervention, and we believe that conservative treatment with PDRN alone may not be appropriate in patients with an ABI of 0.9 or less.

In previous clinical studies applying PDRN, PDRN was applied almost daily (5 d a week) by various routes (perilesional or intramuscular)[17,18], but it is difficult to apply it 5 d a week in reality due to economic problems, but in this case, we demonstrate that only once a week perilesional injection is effective.

The dorsal surface of the foot is characterized by the presence of tendons just below the thin soft tissue, and wounds exposing the tendons are difficult to reconstruct with relatively minor surgery such as split-thickness skin graft (STSG) due to poor vascularity of the tendons[19]. In addition, due to the poor vascularity of the tendon, tissue granulation and epithelialization are difficult, making reconstruction difficult even with conservative treatment. As observed in Case 1 above, if the tendon is exposed, sacrifice of the tendon may be considered if damaged, non- functional and unlikely to result in significant comorbidity.

When performing STSG reconstruction on a wound with tendon exposure, it has been reported that flipping the tendon over allows for better STSG uptake due to the presence of vascularized connective tissue[19]. Therefore, if it is difficult to sacrifice the tendon, it is possible to consider applying PDRN after flipping the tendon to expose the vascularized connective tissue.

In these cases, PDRN was used following debridement of all necrotic and inflammatory tissue and resulted in successful healing of a diabetic foot ulcer. We demonstrate that thorough wound care and proper debridement are critical because infection impairs wound healing. There were no adverse events recorded during this study period, indicating that PDRN treatment was safe and tolerable.

## CONCLUSION

This study demonstrates that if the patient declines surgical intervention for diabetic foot ulcers on the dorsum of the foot with Wagner grade II or below, conservative treatment with PDRN injection can be successful as long as the poorly vascularized tissue is removed and the wound bed is maintained clean. The favorable response of the patient to PDRN therapy shows its potential as an effective and safe solution for non-healing foot wounds. Larger prospective trials will be



**Figure 3 Case 1, post-treatment photograph.** After treatment with polydeoxyribonucleotide injection for 8 wk, the raw surface area was healed and epithelialized without exposure of muscles and tendons.




**Figure 4 Case 2, post-treatment photograph.** After treatment with polydeoxyribonucleotide injection for 6 wk (left) and 8 wk (right), the raw surface was almost healed by 6 wk and completely healed and epithelialized without exposure of muscles by 8 wk. A: After treatment with polydeoxyribonucleotide injection for 6 wk; B: After treatment with polydeoxyribonucleotide injection for 8 wk.

required to demonstrate the efficacy of PDRN.

The lack of a control group and the inclusion of only two patients are two of the limitations of this case study. The lack of a control group limits our ability to make definitive conclusions about the advantages of PDRN therapy over other modalities. Furthermore, the patient's specific wound characteristics might limit the findings' generalizability to a broader patient group.

## FOOTNOTES

**Author contributions:** Kwon H performed the research; Ha Y and Kim JH wrote the manuscript (original draft); Kim J and Kwon H wrote the manuscript (reviewing and editing); All authors have read and approved the final manuscript.

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