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Reconstructive

Hybrid Regenerative Therapy for Successful Reconstruction of an Infected Traumatized Diabetic Foot Wound

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Summary: Diabetic foot ulcers are a significant complication of diabetes, affecting millions globally, and require appropriate antibiotics, surgical debridement, wound care, and metabolic optimization for management. This article presents an innovative hybrid regenerative therapy for reconstructing an infected, traumatized foot wound of a 62-year-old man with diabetes mellitus who presented with a week-old injury after a car accident. At presentation, he had a 14×10cm dorsal foot wound with skin necrosis, pus discharge, and bony instability owing to partial fractures and joint dislocations. Antibiotics were administered to treat multidrug-resistant bacteria and followed by surgical debridement and the application of a portable Velnext negative pressure wound therapy device. Once the wound condition stabilized, hybrid regenerative therapy was performed weekly. Six milliliters platelet-rich plasma and 6mL platelet-poor plasma were prepared from 27mL of venous blood mixed with 3mL sodium citrate and injected into the tendons, soft-tissues, and muscles. Next, the exposed bones and tendons were covered with platelet-rich fibrin and semi-occlusive membranes, and a Velnext negative pressure wound therapy device was applied over them. The wound improved progressively during the subsequent 6 weeks and was finally covered with a split-skin graft. The patient had a successful 18-month postoperative period until now with stable grafts, anatomical restoration, and excellent foot functionality. Thus, hybrid regenerative therapy, encompassing several prevalent methods for healing wounds, has excellent benefits for treating complex diabetic foot ulcers. *(Plast Reconstr Surg Glob Open 2023; 11:e5213; doi: 10.1097/GOX.0000000000005213; Published online 16 August 2023.)*

INTRODUCTION

Diabetes mellitus affects over 500 million people worldwide, with diabetic foot ulcers (DFUs) being a major complication. DFUs have high chronicity and morbidity and are often complicated by infections, leading to osteomyelitis and amputations. Associated comorbidities decrease immunity and wound healing.[1] The 5-year survival rate for diabetes-related amputations is 40%, surpassing the mortality rate of many cancers.[2]

Treatment goals for DFUs include avoiding amputation, controlling infections, preserving deep-tissues, and minimizing healthcare requirements while improving general condition. Here, hybrid regenerative treatment, amalgamating and modifying prevalent techniques, ensured robust soft-tissue regeneration while healing an infected and injured diabetic foot wound [**See Video (online)**, which displays the details involved in hybrid regenerative therapy].

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Presentation

A 62-year-old man with diabetes mellitus presented to the hospital with fever, acute diabetic foot disease, and a 1-week-old left foot injury from a car accident. He had a history of coronary artery stenting and a mild stroke. Foot radiograph showed first metatarsal fracture and tarsometatarsal dislocation with scattered particles. [**See figure 1, Supplemental Digital Content 1,** which displays foot radiograph showing partial fracture of the first metatarsal bone (white arrow head), first tarsometatarsal joint dislocation, and scattered dirt particles all around (black arrow heads). **http://links.lww.com/PRSGO/C754**.] Examination revealed significant dorsal foot injury with skin necrosis, pus discharge, and

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Fig. 1. A 14×10 cm dorsal foot wound was observed with exposed tendons, partially fractured bones, unstable tarsometatarsal joints, and periosteal necrosis.

bony instability, including partial fractures and periosteal necrosis (Fig. 1). The patient had pyrexia, tachycardia, tachypnea, and anemia, with HbA1c of 7.2 and fasting blood glucose of 149 mg per dL. He had been prescribed linagliptin 2.5 mg and metformin 500 mg, but intentional nonadherence hampered recovery. Echocardiography showed reduced ejection fraction and bi-ventricular systolic dysfunction, whereas Doppler examination revealed adequate blood flow but poorly defined lower leg perforators.

Initial Management

Microbial tissue culture revealed multidrug-resistant *Pseudomonas aeruginosa* and extended-spectrum beta-lactamase-producing *Escherichia coli*. Meropenem and colistin were administered for 7 days after sensitivity results. After surgical debridement, a portable negative pressure wound therapy (NPWT) device (Velnext, Datt Mediproducts, Delhi, India) was applied to the 14×10 cm wound. Four days later, the wound exhibited dry, shriveled, yellowish tendons, and minimal granulations. (**See figure 2, Supplemental Digital Content 2**, which displays that 4 days after standard NPWT therapy, a dry wound with shriveled, yellowish tendons, and minimal granulations were seen. **http://links.lww.com/PRSGO/C755**.) To maintain moisture, the tendons were then covered with semi-occlusive films before applying NPWT. After another 4 days, the wound showed improvement with healthy tendons and reddish granulations. The patient, after careful consideration about reconstructive surgery options, opted for a minimally-invasive approach and underwent hybrid regenerative therapy.

Hybrid Regenerative Therapy

Six milliliters of platelet-rich plasma (PRP) and 6 mL of platelet-poor plasma (PPP) were obtained after centrifuging 27 mL of venous blood admixed with 3 mL of sodium citrate after established protocols.[3] PRP was injected superficially into the tendons and adjoining soft-tissues, whereas PPP was injected intramuscularly (Fig. 2). Platelet-rich fibrin (PRF) membranes were placed over the tendons and covered with a semi-occlusive membrane fenestrated over the raw areas but left intact over the tendons and bones. Finally, the wound was covered with

Takeaways

Question: How can complex wounds be reconstructed with sufficient soft-tissue regeneration without using flaps or biomaterials?

Findings: A hybrid regenerative therapeutic approach consisting of platelet-rich plasma, platelet-poor plasma, platelet-rich fibrin, semipermeable membrane, and a portable negative pressure wound therapy device proved to be successful in treating a complex diabetic foot ulcer. By modifying negative pressure wound therapy and placing semipermeable membranes over tendons and bones to preserve moisture, substantial soft-tissue regeneration was achieved without the need for flaps or biomaterials.

Meaning: Hybrid regenerative therapy may efficiently heal complex wounds with exposed bones and tendons, resulting in stable wound cover and excellent functionality.

Fig. 2. PRP, prepared from venous blood, was injected into the exposed tendons and surrounding subcutaneous tissues.

Fig. 3. Substantial soft-tissue regeneration was seen over the wound, covering all exposed bones and tendons, after hybrid regenerative therapy.

Velnext NPWT and suctioned continuously for 7 days. This process was repeated weekly for the next 6 weeks [**See Video (online)**].

Results

Weekly wound explorations showed progressive improvements without deteriorations or infections. The wound shrunk, tendons healed, and voluminous

Fig. 4. After a split-skin grafting, good anatomical and functional restoration of the injured left foot was observed.

granulations covered the sizeable wound (Fig. 3). A split-skin graft was applied and healed within a week (Fig. 4). After physiotherapy, the patient regained mobility, resumed work, and showed normal movements on gait analysis. He reported an excellent 10/10 on a visual analogue patient-reported outcomes scale. An 18-month postoperative period was uneventful, with stable grafts, anatomical restoration, and excellent foot functionality [**See Video** (**online**)].

DISCUSSION

DFUs are a common and dangerous consequence of diabetes, resulting from various factors such as repetitive trauma, poor glycemic control, and neuropathy. Associated immune deficiencies cause rapid deep-tissue infections through skin ulcers.[4] *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli*, and *Enterococcus* are common isolates.[5] Diagnosis involves clinical evaluation, culture/sensitivity, radiographs, and imaging. Effective management of DFU includes antibiotic therapy, surgical debridement, wound care, and metabolic optimization.[4]

Muscle flaps are commonly used for reconstructing infected wounds due to their ability to enhance blood flow and fill dead spaces. However, in diabetic patients with poor lower extremity circulation, using muscle flaps for large DFUs becomes challenging. Muscle flaps are associated with complications such as flap loss, hematoma, seroma, infections, scarring, fat necrosis, wound dehiscence, and delayed healing, making them less desirable in certain cases.[6]

The traditional approach to foot wound treatment involves moist-to-dry dressings and skin grafting. However, its limitations include prolonged healing time, infection risk, pain, and difficulty in generating good granulations when tendons, bones, or implants are exposed. Some surgeons resort to removing extensor tendons and using NPWT or moist dressings to promote granulation, leading to permanent disability and foot deformity.[7] Tissue scaffolds are effective but were unavailable due to COVID-19-related supply chain disruption, posing a significant challenge in treating this patient's injured and infected foot.

NPWT offers advantages over traditional wound care, including lower infection rates, faster healing, and decreased amputation risk in diabetic foot wounds. It creates a moist wound environment, removes inhibitory factors, and promotes healing.[8] Semi-occlusive dressing induces secretomes in wound fluids, modulating the healing process by maintaining moisture for autolytic debridement, collagen synthesis, and keratinocyte migration. Additionally, it enhances the function of growth factors, cytokines, and nutrients in the wound microenvironment.[9]

PRP injections mimic the natural wound-healing process by utilizing platelets as initial responders. Typically, 2–6 mL of PRP is directly injected into the injured tendon, often guided by ultrasound. They effectively heal tendinopathies and contribute to the development of "orthobiologics." Numerous studies demonstrate the pain-reducing and function-improving effects of PRP injections in various tendon injuries. PRP's growth factors promote tenocyte proliferation and accelerate healing, thereby improving tissue quality of healing tendons.[10]

PRP accelerates soft-tissue regeneration and wound healing, effectively treating DFUs in 8 weeks without adverse effects. Combining PRP with adipose-derived stem cells enhances healing rates of chronic skin ulcers.[11] PRF, a second-generation platelet concentrate, promotes wound healing, reduces repair time for chronic injuries, facilitates bone regeneration, contains immune cells, and exhibits antimicrobial effects against specific bacteria.[12]

CONCLUSIONS

Hybrid regenerative therapy combines surgical debridement with PRP and PPP injections, PRF, semi-occlusive membrane application, and NPWT therapy. This approach was used weekly in a 62-year-old man with diabetes mellitus, resulting in successful healing of a complex foot wound. It achieved outcomes similar to those achieved with muscle flaps and tissue scaffolds but with reduced risks, complications, and costs, offering potential benefits for successfully healing complex diabetic foot wounds globally.

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DISCLOSURE

The author has no financial interest to declare in relation to the content of this article.

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