

Adjuvant platelet-rich plasma after lower extremity revascularization for treatment of foot ulcer: a case report

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ABSTRACT

In patients with plantar ulcers, both diabetes and peripheral occlusive disease are implicated in the disease process, resulting in diminished blood flow to the extremity and, thereby, interrupting or delaying the wound healing process. The risk of amputation is extremely high in diabetic patients with plantar foot ulcers-related limb ischemia. Herein, we report a diabetic case in whom adjuvant platelet-rich plasma therapy was applied following surgical revascularization of the plantar foot ulcer.

Keywords: Healing; peripheral artery disease; platelet-rich plasma; wound.

Severe chronic wound ulcers of the lower extremity may cause serious disability when located in the plantar surface of the foot, particularly.^[1] In patients with plantar ulcers, both diabetes and peripheral occlusive disease are implicated in the disease process, resulting in diminished blood flow to the extremity and, thereby, interrupting or delaying the wound healing process.^[1] Diabetic plantar foot ulcers has also distinct pathological features such as fat pad atrophy due to irregular arrangement of collagen fibrils and distal fat pad migration which renders the metatarsal heads susceptible to pressure and eventually leads foot ulceration.^[1]

Platelet-rich plasma (PRP) has been in use for promoting healing of surgical wounds for nearly two decades.^[1] Application of PRP to chronic wounds has recently gained popularity and several reports have appeared in the literature regarding its effectiveness in diminishing the wound area.^[1] There is also a growing evidence showing its benefits in patients with diabetic foot ulcers.^[2]

Herein, we report a diabetic case in whom adjuvant PRP therapy was applied following surgical revascularization for plantar foot ulcer.

CASE REPORT

A 71-year-old diabetic male patient presented with critical limb ischemia and deep foot ulcer located at the plantar surface of the left foot lasting for about six months. The patient suffered from chronic

hypertension, renal failure (i.e. serum creatinine: 2.18 mg/dL), chronic ischemic heart disease and had a 15-year-history of diabetes receiving long-acting insulin. He had a long-standing history of reduced walking distance before ulceration of the wound and received only pharmacological therapy without being operated on for peripheral arterial occlusive disease. He had also lower extremity numbness and pain in toes for more than five years. He had no history of major or minor extremity amputation and underwent multi-vessel coronary artery bypass grafting three years ago alone and also had a recent transient ischemic attack. Systolic heart functions were normal. The patient was consulted for the decision on the level of amputation.

On physical examination, there were severe trophic changes and desquamation on toes which suggested severely diminished blood flow and the presence of an untreated chronic fungal infection. The extremity was cyanotic and cold; however, motor neuron functions were intact. The wound was 10 cm² in surface area and was approximately 8 mm in depth (Figure 1a). There was excessive fibrosis around the inner surface of the wound. The loss of fat pad tissue was so severe that even metatarsal heads were visible. Ankle systolic pressure was below 35 mmHg, indicating severe critical limb

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ischemia. The patient was admitted to the department of cardiovascular surgery to achieve limb salvage and initiated on standard therapy including intravenous fluids, broad spectrum antibiotics (ciprofloxacin 500 mg per day), subcutaneous low-molecular-weight heparin, and peroral pentoxifylline.

Wound swab cultures were taken and the wound was debrided under sterile conditions for removal of necrotic tissues. The wound swab cultures were contaminated and no specific microbial agents were able to be isolated. Antibiotic treatment was continued and local anti-fungal spraying was added to the treatment. Contrasted computed tomography showed an interrupted contrast enhancement along a 10 cm segment within the left superficial femoral artery and distal bed (tibial arteries) poorly filled with contrast agent due to multi-segmental atherosclerotic lesions of tibial arteries.

Under spinal anesthesia, we performed a left femoropopliteal artery bypass using 7 mm diameter ringed expanded-polytetrafluoroethylene graft with the distal anastomosis being located on the popliteal artery as distal as possible - just distal to the Hunter's canal. After the operation, tibialis anterior artery was not palpable; however, a stronger biphasic flow was achieved on the artery and the ankle systolic pressure increased up to 50 mmHg.

The patient received two sessions of PRP therapy beginning on the day after the operation and the therapy was repeated one week after the beginning. During this therapy, surface of the wound was washed with physiologic saline and hypochlorous acid was used to clean the healthy tissue around the wound. Platelet-rich plasma was prepared using Easy PRP KIT system (Neotec Biotechnology, Istanbul, Turkey). Twenty milliliter of venous blood was taken from



Figure 1. (a) Wound at plantar surface of the foot on admission. (b) Healing process. (c) About 70% reduction was achieved at five weeks after surgery with platelet-rich plasma treatment.

antecubital vein and added into a 9/1 acid citrate dextrose containing test tube under aseptic conditions. The tube was centrifuged at a rate of 5000 rpm for 15 minutes to separate red blood cells from platelets and plasma. Platelet containing plasma was harvested by collecting platelet and plasma containing supernatant and thin white layer and it was centrifuged at a rate of 2000 rpm for five to 10 minutes. The 2 to 3 mL bottom layer was collected and added to 0.3 mL of 10% calcium chloride for each 1 mL of PRP. A 10 mL of PRP substance was administered into the wound with half of the amount being injected 1 to 2 mm deep into the wound and then the wound surface being covered with the remaining half. The lesion was covered with soft silicone polyurethane foam dressing (Mepilex®, Göteborg, Sweden) which was used in the treatment of diabetic foot ulcers previously. The wound dressing was changed every other day and the wound was only rinsed with physiological saline.

The patient did not receive any other type of wound care or therapy. After discharge, he was invited for weekly follow-up (Figure 1b). The patient had around 70% reduction in the wound area within five weeks after the operation (Figure 1c). As he was living in a distant rural town, he did not attend to follow-up any longer and reported that his wound completely healed during phone interview.

DISCUSSION

Our patient benefited from adjuvant PRP following surgical revascularization for the treatment of severe foot ulcer. Given the patient's poor limb status on admission and various risk factors, both treatment modalities seems to prevent an otherwise unavoidable major amputation. The procedure was safe, as it did not result in any deterioration in the wound status. The preparation and application of the substance was also simple and cost-effective. Although surgical or endovascular revascularization is still the mainstay in the treatment of critical limb ischemia regardless of the presence of wound lesions, limb prognosis is still poor in patients with diabetes and infection. Therapeutic angiogenesis with stem cells, growth factors, and autologous progenitor cells have been used to treat critical limb ischemia patients to achieve improvement in wound healing; however, all these therapies had their own limitations and research continues for adjuvant therapies which would promote wound healing after revascularization.^[3]

In recent years, the importance of a multidisciplinary approach in the treatment of diabetic foot ulcers has increasingly become recognized. A recent Spanish registry study showed that the introduction of a multidisciplinary team coordinated by an endocrinologist and a podiatrist for managing diabetic foot ulcers yielded a significant reduction in the incidence of major lower extremity amputations in diabetic patients.^[4]

In an experimental model, platelet-rich fibrin matrix, a variant preparation with similar properties, induced endothelial cell proliferation, suggesting an explanation of wound healing effect of PRP.^[5] In a clinical study including 17 patients with chronic wounds of different etiologies receiving PRP therapy, Roubelakis et al.^[6] reported that the majority of wounds were of diabetes and ischemic etiology and also were infected or necrotic. The mean volume reduction was 34.1% in all types of ulcers within eight weeks through a mean separate PRP session of 9.5. This study provided evidence that PRP regulated wound healing by acting on cell migration and proliferation.

The use of PRP in the treatment of non-healing diabetic foot ulcers has not been studied widely. There have been only a small number of case reports or case series in the literature. Mehrannia et al.^[7] reported a 71-year-old male case with severe diabetic wounds in both soles of his foot which showed improvement after application of PRP. In consistent with our findings, the authors performed deep injection through the wound, although the peripheral arterial status of the patient was not mentioned.

In another 57-year-old diabetic male case with non-healing wound on his left foot for four years, Suresh et al.^[8] also used PRP in a similar way to our application. The wound was the stump of the amputated left toe. The patient received six sessions of PRP and achieved complete healing.

In another recent study including diabetic patients with concomitant peripheral artery disease, Kontopodis et al.^[9] investigated whether PRP improved healing of diabetic foot ulcers. In this study, 30 of 72 patients had critical limb ischemia and a total of 52 patients had ulcer reduction after receiving PRP treatment. Based on their findings, the authors concluded that PRP might serve as a useful adjunct during the management of diabetic foot ulcers even in diabetic patients with severe non-reconstructable peripheral artery disease.

In conclusion, the adjuvant use of PRP to promote wound healing after revascularization for critical limb ischemia seems promising in terms of preventing future amputations. As our patient had a marked increase in ankle systolic pressure and apparently benefited from surgical revascularization, we cannot draw a conclusion suggesting the role of PRP in achieving complete healing. Nevertheless, given the depth of the ulcer and various comorbidities our patient had, PRP might at least accelerated the wound healing process, eliminated the need of additional attempts for wound care, and possibly prevented the dissemination of the infection which might further lead amputation of the extremity.

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