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Case Report

Platelet-Rich Plasma: A Promising Therapy for Recalcitrant Venous Leg Ulcer: A Case Report

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ABSTRACT

Venous disease is the most common cause of leg ulcers with considerable morbidity and a dramatic negative impact on patient's quality of life. Platelet-rich plasma (PRP) is an autologous preparation of platelets in concentrated plasma and contains various growth factors that can modulate healing process. PRP is a simple, safe, affordable procedure for venous ulcer which is therapeutically challenging. Herein, we report a case of recalcitrant non-healing venous leg ulcer treated effectively with PRP therapy and discuss about the promising possibility of autologous PRP as an effective alternative therapeutic modality.

Keywords: Platelet-rich plasma, venous ulcers, non healing.

INTRODUCTION

Venous leg ulcers are responsible for more than half of lower extremity ulcerations, with prevalence ranging from 0.06% to 2%. [1] Conventional therapies cannot provide satisfactory healing since these treatments are not able to provide necessary growth factors that can modulate healing processes. [2,3] PRP therapy represents a greater similarity to natural healing process as it is a composite of multiple growth factors. [4]

PRP (also referred to as platelet enriched plasma, platelet rich concentrate, autologous platelet gel and platelet releasate) is a volume of autologous plasma that has a platelet concentration above baseline, five times more than the normal platelet counts. [4,5]

CASE REPORT

A 55yr old male presented with two non healing ulcers on left leg since 3yrs. He gave past history of surgery for sapheno-femoral incompetence followed by split-skin grafting 2yrs back. But the graft failed to take up and the ulcers recurred. Since then, he had been treated with regular ulcer debridements and other supportive measures. But the ulcers failed to heal and continued to deteriorate which affected the quality of life of the patient both at his home and workplace.

On examination - Left leg showed 2 ulcers with well defined margins, sloughy floor and sloping edges [Figure 1].

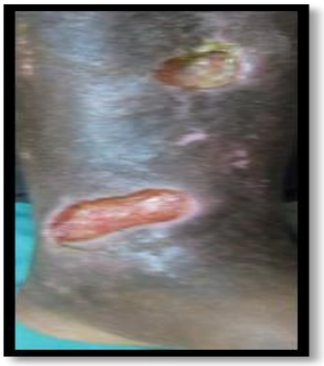

Figure 1: Initial presentation of the two ulcers on left leg.

Ulcer 1 was shallow, 7 cms x 5 cms in size situated on medial malleolus [Figure2]. Ulcer 2 was deep with exposed bone, measuring 4 cms x 3 cms on the middle third of shin [Figure 3]. Signs of chronic venous hypertension such as edema, lipodermatosclerosis, hemosiderin staining and atrophie blanche were present on the lower one third of the left leg.

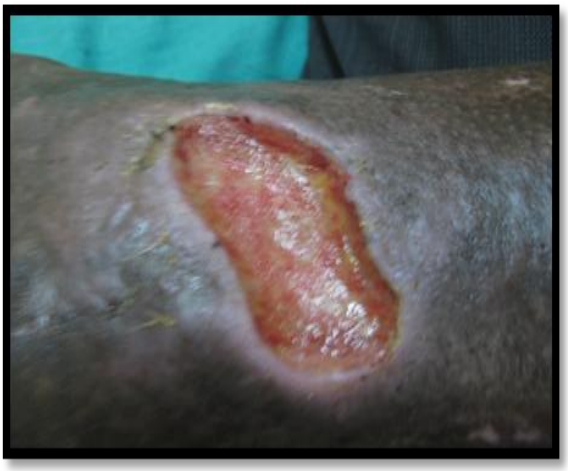

Figure 2: Ulcer 1 on medial malleolus.

Venous doppler study done for the left leg showed two incompetent perforators, one above and one below the ankle. X-ray of the left leg showed diffuse periosteal reaction involving metadiaphyseal region of both left tibia and fibula, secondary to venous stasis. Pus culture sensitivity from the ulcer showed growth of staphylococcus aureus sensitive to amikacin. Blood investigations were done to rule out any co-morbidities and other causes of chronic leg ulcer including serology for syphilis, antinuclear antibody and screening for retroviral disease.

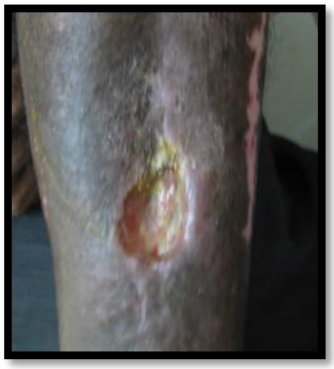

Figure 3: Ulcer 2 on the shin with slough.

Diagnosis of chronic recalcitrant venous leg ulcer was made and autologous PRP therapy was initiated along with other supportive measures. PRP was prepared by double spin method.

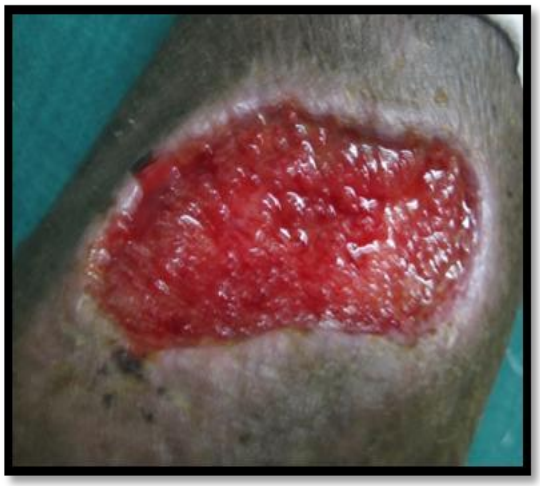

Figure 4: Ulcer 1 at the end of second week showing red granulation tissue

10 ml of venous blood drawn under aseptic precautions into test tubes containing

acid citrate dextrose anticoagulant was first centrifuged at 5000 rpm for 15 mins, to separate the red blood cells from the platelets and plasma. The supernatant and buffy coat was collected and centrifuged again at 2000 rpm for 10 mins. The upper 3-4 ml of platelet poor plasma was removed. 10% calcium chloride was added (0.3 ml for 1 ml of PRP) to activate the platelets. The resultant activated PRP was applied onto the ulcers, after proper surgical debridement and was dressed with non-absorbent dressing. This process was repeated once weekly

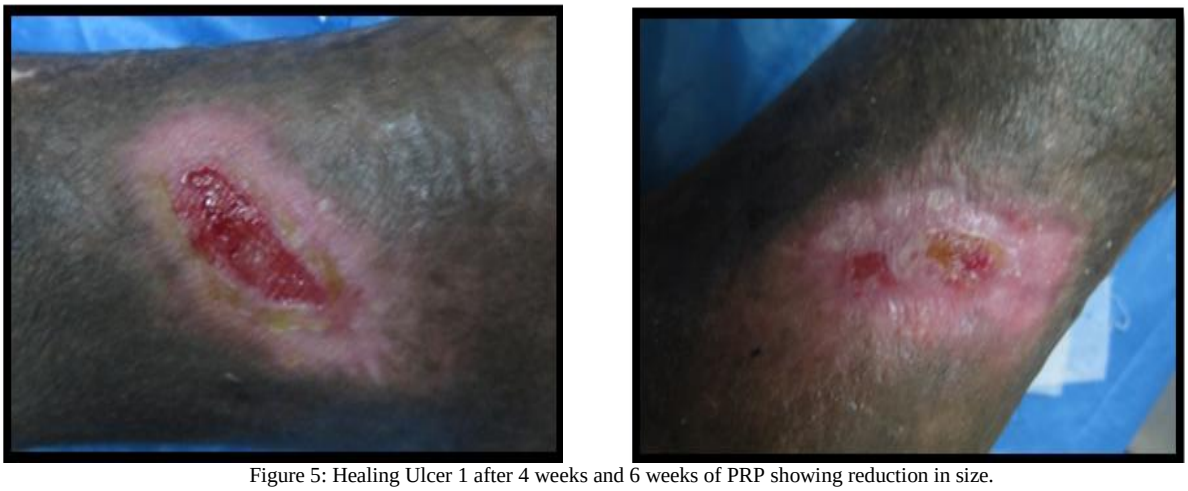

Figure 5: Healing Ulcer 1 after 4 weeks and 6 weeks of PRP showing reduction in size.

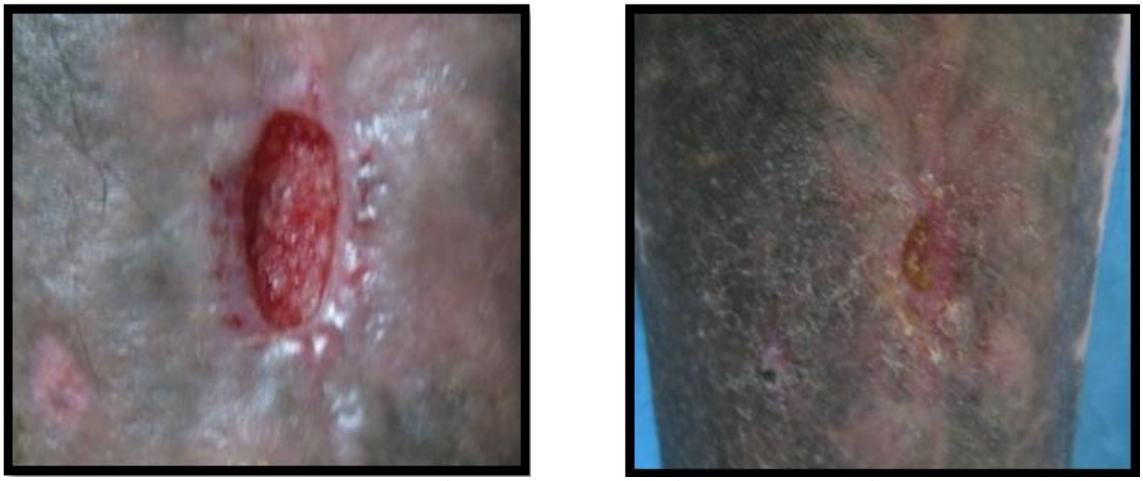

Figure 6: Ulcer 2 after 4 weeks and 6 weeks of PRP showing signs of healing.

Over the course of 8 weeks, the ulcer beds became vascularised, filled with red granulation tissue [Figure 4]. Reduction in wound surface area and depth were noted during the course of therapy for both ulcer 1 [Figure 5] and ulcer 2 [Figure 6].

After 8 sittings of PRP dressings, both the ulcers healed well with epithelisation at the end of 2 months [Figure 7].

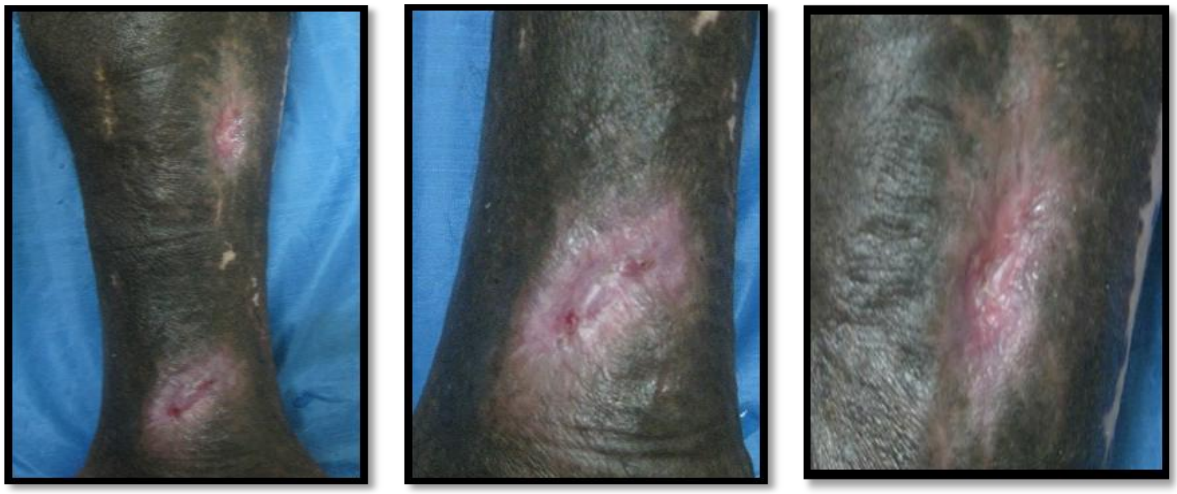

Figure 7: Healed ulcers at the end of 8 PRP dressings.

DISCUSSION

A platelet concentration of more than 1 million/μL is generally regarded as the therapeutically effective concentration of PRP. Giusti *et al*., demonstrated that lower or higher concentrations than 1.5 million platelets/μL, seemed to inhibit the angiogenic potential in human endothelial cells. [6,7]

PRP – The Growth Factor agonist

The cocktail of growth factors (GFs) in PRP by virtue of platelets alone (stored as alpha granules in platelets) are platelet derived growth factor (αα, αβ, ββ), transforming growth factor-β1, β2, vascular endothelial growth factor, epidermal growth factor, hepatocyte growth factor, fibroblast growth factor. These GFs are pivotal in modulation of tissue repair and regeneration. The plasma proteins in PRP, namely, fibrin, fibronectin and vitronectin act as scaffold for the bone, connective tissue and epithelial migration. [8]

Mechanism of action in acceleration of wound healing

Degranulation of the pre-packaged GFs in platelets occurs upon "activation" i.e., on coming in contact with coagulation triggers. The secreted GFs in turn bind to their respective trans-membrane receptors expressed over adult mesenchymal stem cells, osteoblasts, fibroblasts, endothelial cells, and epidermal cells.[6] This further induces an internal signal-transduction pathway, unlocking the expression of a normal gene sequence of a cell like cellular proliferation, matrix formation, osteoid production, collagen synthesis, angiogenesis, mesenchymal cell recruitment, proliferation and extracellular matrix synthesis, thereby augmenting the natural wound-healing process. [2,6] Studies of PRP have demonstrated anti-microbial property and role in host defence mechanism at the wound site by producing signaling proteins that attract macrophages. [4]

Advantages of PRP

Being an autologous preparation, PRP is safe to use and free from concerns over transmissible diseases and antibody formation, thus leading to better acceptance by patients. The small blood draws for PRP do not have an effect on haemoglobin, haematocrit, or platelet count. [4] The mitogenic effects of PRP are only limited to augmentation of the normal healing process and is theoretically not mutagenic, as the growth factors released do not enter the cell or nucleus, but only bind to the membrane receptors and induce signal transduction mechanisms. [6]

CONCLUSION

Though there are no double blind, randomised, placebo controlled trials conducted on a large sample size to constitute a good quality of evidence or standardisation of procedure, the potential role of PRP in dermatology and aesthetic medicine is an exciting frontier that may eventually lead to superior therapies in near future. Overall, PRP therapy is a promising, safe, biocompatible, simple, inexpensive, effective therapy for faster healing of recalcitrant venous leg ulcers which are therapeutically challenging. Our case report shows the favourable outcome of the chronic recalcitrant venous leg ulcer using autologous PRP therapy.

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