

The Efficacy of Platelet-rich Plasma Combined with Platelet-rich Fibrin in the Treatment of Multiple Chronic Venous Leg Ulcer: A Case Report

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Abstract : Chronic leg ulcer (CLU) is a defect in the skin below of knee persisting for more than six weeks and shows no tendency to heal after three or more months. Leg ulcers occur in 1% of the adult population and 3.6% in people over 65 years. It may increase with the onset of aging, people with atherosclerotic occlusion such as smoker, obese and diabetic. A 55 years old woman, came with multiple ulcer in her left leg since 5 years ago. There were various size of ulcers in her left leg, the largest size was 12x 9x 0.1 cm and the smallest one was 6x 6x 0.1 cm with erythema base. On examination ankle brachial index (ABI) was 0.9. Patient was diagnosed with deep vein thrombosis (DVT) since 5 years ago, with no satisfying treatment. Compression therapy is still the basic treatment for venous ulcers, but in our case, compression therapy was not given satisfactory result. Platelet-rich plasma (PRP) and platelet-rich fibrin (PRF) autologous are some of the therapies that we can use in chronic wounds. Autologous PRP and PRF are contain many growth factors (GF), that can help the healing process in chronic wounds, the treatments are easy to use, painless and safe. In our case we used combined therapy of PRP and PRF for treating CLU and we also used intralesional PRP injection for the initial treatment and results in satisfying improvement after 13 weeks observation.

1 INTRODUCTION

Chronic leg ulcer (CLU) is characterized with a chronic wound in the leg without healing after 3 months with proper treatment or not recovering optimally at 12 month. Chronic leg ulcer (CLU) common in adults and the symptoms usually include pain, friable granulation tissue, foul odor, and wound breakdown instead of healing. This result social distress, considerable healthcare and personal costs (Shubhangi, 2013). In Chronic wound as in CLU the levels of platelet derived growth factor (PDGF), basic fibroblast growth factor (bFGF), epidermal growth factor (EGF), and transforming growth factor (TGF-) is reduced (Sebastian, 2007).

Venous ulcer is the most common type of chronic ulcer, with the incidence of 1-2 % in the population. It is 75-80% of all vascular ulcers (Braund, 2007). Heredity, age, female sex, obesity, pregnancy, prolonged standing, and greater height are the risk factors for the venous disease. At early

presentation, tenderness, edema, hyperpigmentation, and varicose veins are typical features, at later stage, atrophy blanching, lipodermatosclerosis and venous ulcers (Burkhart, 2008). Ankle Brachial Index (ABI) score is usually used for assessing patient with lower extremity venous insufficiency, the lower score, means the more severe the arterial obstruction (Sebastian, 2007). The conventional treatments of vascular ulcers are leg elevation, compression, and wound care. Topical steroids, aspirin, and surgery are as second-line therapies. Autologous platelet-rich plasma (PRP) is one of many treatment for chronic leg ulcer, and it is promising therapy (Braund, 2007).

PRP is a concentration of platelets required from the patient's own blood which has been in centrifugation. It contains fibrin and high concentrations of growth factors (Yotsu, 2015). A second-generation in platelet concentrate is PRF, it is prepared from centrifuged blood, during preparation we can find a fibrin clot rich in platelets

without addition of thrombin, platelet-derived growth factor and TGF- β has been identified in PRF. Platelet-rich plasma (PRP) and PRF speed up wound healing by promoting the healing process secondary to its GF. These include platelet-derived GF ($\alpha\alpha$, $\beta\beta$, and $\alpha\beta$) fibroblast GF, vascular endothelial GF, epidermal GF, insulin-like GF, and transforming GF, which are needed in chronic wound healing (Suthar, 2018).

2 CASE

55 years old woman presented to the Dermatovenereology Outpatient of Dr. Moewardi General Hospital Surakarta with chief complaint of multiple ulcer in her left leg since 5 years ago. Itchy red spot appeared on her left leg, which later became small wound and her leg skin changed into black. The wound then enlarged as the time went by. She then sought medical help and was diagnosed with stasis dermatitis. After 2 months there was no improvement, she came back to the same hospital and she was treated by internist as she was diagnosed with DVT confirmed USG Doppler, after 3 months of treatment with elastic bandage (compression), aspirin^R and venosmil^R without

improving, a new small wound appeared in the same leg. Because the wound enlarged, the doctor referred patient to vascular surgery, and she had debridement. She came back to her internist and she was received additional therapy with simaric^R, amlodipine and candesartan^R. However, the therapy did not give satisfactory result, which made her to come to our clinic.

This patient works as a shopkeeper who required to stand for a long time. Physical examination revealed high blood pressure 160/100 (hypertension grade 1), Body Mass Index (BMI) 26.6 (Obesity I), the dorsalis pedis artery pulse was well palpable and there was no specific finding in the laboratory examinations.

The dermatological examination demonstrated, multiple ulcer with the largest size of 9.5x 13x 0.1 cm and the smallest one 6.5x 6.5x 0.1 cm, at her left leg varicose vein, hemosiderin and lipodermatosclerosis also seen.

We treated the patient with PRP injection 0.2cc/cm² for initial therapy, after that we used the topical PRP in antioxidant gel and we combined with PRF for maintenance. We observed the patient in every 3 days for 8 weeks months after that we once a week. After 13 weeks of observation there was satisfactory improvement.



Figure 1. (A-C). Multiple ulcer with the bigger size is 9.5x 13x 0.1 cm and the smallest size is 6.5x 6.5x 0.1 cm. (D-F) 13 weeks of therapy with PRP combined PRF given every 3 days for 8 weeks, after that we once a week monthly.

3 DISCUSSION

One of the up to date modalities for CLU is PRP (Hafner, 2012). Platelet-rich plasma (PRP) research has long been studied for its the molecular interaction of platelets and plasma secretion with different cell phenotype. Platelet-rich plasma (PRP) is promising therapy in wound care, as it increases cell migration, proliferation, angiogenesis, and tissue anabolism. Safe because free from antibody formation, graft versus host's disease and infectious diseases such as hepatitis and HIV, easy and cost-effective method with good results in the management of chronic non healing ulcers are an advantages of autologous PRP (Alavi et al, 2016). Aside from PRP we can use PRF, it also contains fibroblast growth factor (GF), vascular endothelial GF, angiopoitin and platelet-derived GF. These speed up the wound healing (Andriessen, 2017). He L, et al in the statistical analysis levels reported that TGF- β and PDGF-AB released from PRF or PRP at different time points. PRP released the highest amounts of TGF- β and PDGF-AB at the first day, followed by significantly decreased release at later time points PRF released the highest amount of TGF- β at day 14th and the highest amount of PDGF-AB at day 7th (He, 2009). Choukroun et al. is the first who develop PRF in France to be used in oral and maxillofacial surgery, PRF belongs to a new generation of platelet concentrates with simply preparation and without any biochemical blood handling (Nagaraju, 2017). The intralesional injection of platelet concentration constitutes a valuable alternative in the treatment of chronic ulcers (Suthar, 2018).

Handling all possible systemic and local factors which can interrupt healing process is the first step in treating ulcers (Hafner, 2012). Next eliminating or treating the causes of precipitation, such as, surgical intervention, until promotes circulation and improves venous return, for example, compression therapy. Wound care, lifestyle changes and symptom management are needed for healing. Self-hygiene promote preventive care is very important in preventing its recurrence. Current treatments for CLU include surgery, sclerotherapy, compress therapy (conventional therapy), and adjuvant pharmacotherapy (Shubhangi, 2013). The mainstay treatment for patients with venous leg ulcers is compression therapy, there are 3 different techniques in compression: (1) bandage system, (2) stockings /socks, or (3) intermittent compression device, however there are contraindications in the use of compression therapy high compression of 40 mm Hg

should be considered for a person with an adequate vascular supply indicated by an ankle brachial pressure index of 0.8 to 1.2 and in patients with mixed arteriovenous ulceration (with an ankle brachial pressure index \geq 0.5 and an absolute ankle pressure \geq 60 mm Hg), inelastic compression \geq 40 mm Hg does not impede arterial perfusion and treats impaired venous return (Somani, 2017), (Suryanarayan, 2014), (Moneib, 2017).

Our patient has multiple chronic wounds in her left leg since 5 years ago, without any improvement in the treatment, she was even treated with oral therapy, compression therapy and debridement. The diagnosis of DVT from this patient was confirmed with physical examination, USG Doppler and ABI. Hard to heal wounds are defined as those with granulation tissue which fail to epithelialize despite two months of conservative treatment (Burkhart, 2008). In this case, we can use PRP and PRF for the treatment, as PRP and PRF can improve wound healing through promotion of the healing process by the presence of growth factors which are important in modulating mesenchymal cell recruitment, proliferation, and extracellular matrix synthesis during the healing process (Alavi et al, 2016). Beside PRP and PRF we used injection PRP for the initial therapy, this method accelerates the healing process in the majority of non-healing wounds and contributes to either the complete healing or the preparation of the wound bed for a final reconstructive procedure (Dionysiou, 2012). Platelet Rich Plasma (PRP) combined PRF given every 3 days for 8 weeks, after that we use once a week monthly for 13 weeks. We are not using the compression therapy because our patient felt pain when using the bandage.

4 CONCLUSION

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