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Case Report Open Access

Decubitus Ulcer in a Patient with Non-Hodgkin Linfoma Treated with Topic Collagenase with Hyaluronic Acid and PRP: Case Report and Literature Review

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Abstract

Introduction: Gradual increase in the elderly population in recent years is posing great health challenges and ulcers are one of the major challenges for the patients that are bedridde due to hematologic issues. They are commonly affected by ulcers. Beyond standard treatments, new approach to treat skin ulcers has become the application of topical growth preparations as PRP.

Case Report: We are reporting a case of a 62-year-old male patient affected by non-Hodgkin Linfoma with paraparesis due to a compression over the bone marrow caused due to Linfoma. The prolonged bedridden condition had led to a voluminous class III-IV decubitus ulcer in the sacral region of 20 x 15 cm. We performed a standard medication for the injury for 5 weeks, which consisted in traditional disinfection, cleansing with physiological solution and application of topic collagenase. There was improvement and the wound started healing gradually, when treatmented with 8 cycles of piastrinic gel therapy. After six weeks of PRP treatment, the patient exhibited tremendous improvement.

Production of hemocomponent: The platelet gel was obtained by autologous automatic procedure with multicomponent collection. The platelet count was significantly high and the WBC count was 10 times higher than baseline values of peripheral blood. Cryoprecipitate was obtained and mixed with leucoplatelet concentrate for enrichment and then splitted into 8 small bags. We succeed to reach a high cellular concentration without G-CSF patient stimulation and the procedure was well tolerated by the patient.

Discussion: PRP method consists of collection and concentration of platelets that can release powerful growth-factors and there by cure the wound. Its positive effect is due to released lipoxins, antimicrobial effects, recruitment of undifferentiated cells and promotion of type I collagen formation and MMPs gene expression. It is a cheap and minimally invasive method. A quick review of literature and medical cases reveled the proofs for skin ulcers treated with PRP. This is helpful in treating the present case affected with skin ulcersand the study discusses how this can be managed through PRP application.Conclusion: The study concludes that it is possible to reduce the diameter of the soer and clear the bottom by applying PRP for a patient suffering from non-Hodgkin Linfoma. The study couold prove this treatment as safe with no risk of infection and it improves the quality of life of the patient. This study could establish that PRP application ensures faster healing with minimal or no hospitalization and very low medication.

Keywords: Decubitus ulcer; Autologous PRP treatment; Hematologic patients

Introduction

NPUAP defines the Pressure ulcers as: "localized injury to the skin and/or underlying tissue usually over a bony prominence as a result of pressure, or pressure in combination with shear and/or friction" [1]. 2.5 million pressure sore cases are treated in the United States alone annually [2].

Leg ulcerations are really common in hemolytic anemias, like sickle cell disease. They have a multifactorial etiology, with compromised blood supply as the main factor [3]. Another group of hematologic patients are the one that are affected by the β-thalassemia intermedia, with a prevalence of 8% with leg ulcers [4].

Pressure over prominent bones leading to cuts, skin destruction, and the bleeding are the major symptoms noticed in the physiology path of the pressure ulcers.

Pressure over bony prominence, with a cut, skin destruction and compromised blood flow are the main points in the path physiology of pressure ulcers. New researches brought the evidence that ischemia, more than the pressure, is the main agent that causes pressure ulcers [5].

Gradual rise in the elderly population in recent years has made the skin ulcers a very important problem [6]. Pain management is difficult and the treatment is very expensive [7]. Almost $ 5 billion are spent each year in the US alone to treat these pressure ulcers [8], while the treatment cost for a single wound is $ 70,000 [9].

Debridement, minimization of weight bearing, application of dermal substitutes and VAC therapy are the standard treatments applied to cure o these type of wounds [10-12]. Application of topical growth preparations as an adjuvant treatment is a new approach to treat the skin ulcers [13,14]. This faster way treating the skin ulcers improves the quality of life of the people affected with skin ulcers with reduced cost.

Case Report

62-year-old male patient affected by non-Hodgkin Linfoma appraoched us with the ambulatory of ulcers and severe wounds on March 2011. The patient presented a voluminous class III-IV decubitus ulcer in the sacral region of 20 x 15 cm. The wound was particularly fibrinous with abundant necrotic tissue formation on the surface (Figure 1). CHOP chemotherapy (Cilofosfamide, Doxorubicina, Vincristina, Prednisone) had lead the patient to an advanced stadium of his pathology. The non-Hodgkin Linfoma created a compression over the bone marrow, causing paraparesis which lead to a prolonged bedridden that caused the pressure sore.

Considering the highly precarious condition of the patient, associated with particularly advanced lesion, we have decided to adopt the conservative approach initially. It was based on traditional disinfection with sodium hypochlorite solution of 0,05% (Amukine Med® 0,05%, Amuchina SpA, Genova, Italia) and povidone iodine of 10% (Betadine® 10%, Meda Pharma SpA, Milano, Italia), cleansing with physiological solution and application of topic collagenase (Bionect Start®) with purpose view to reduce the necrotic layer and the superficial fibrosis (Figure 2). This medication was applyed for 5 weeks, 3 times per week at our ambulatory and daily at home.

There was considerable improvement as the wound reduced in size with sores getting dry with 8 layers of PRP application for a period of one week. The patient could not continue this treatment after six weeks as his condition got worsened and was admitted in a hospital, where he died after few weeks (Figure 3).

Anyhow, after 6 weeks of applications of piastrinic gel, a strong melioration of the pressure sore was observed: the diameter of the lesion reduced and the ulcer's bottom clearly improved (Figure 4).

Figure 1: Decubitus ulcer at our first observation.

Figure 2: The ulcer after 5 weeks of treatment with collagenase with hyaluronic acid.

Figure 3: The ulcer with PRP application.

Figure 4: The ulcer after 6 weeks of treatment with PRP.

Production of Hemocomponent

Platelet gel is obtained by autologous automatic procedure with multi-component collection using Haemonetics MCS+® (Haemonetics Corp., Braintree, MA, USA) cell separator and a disposable (code 971E) for peripheral blood stem cell collection using a modified protocol. 60 ml of leucoplatelet concentrate and almost 200 ml of plasma were produced in a span of one hour. The platelet count was significantly high with more than 4,800 x 10^3/µl, the WBC count was 10 times higher than baseline values of peripheral blood.

Cryoprecipitate was obtained from plasma thawed overnight to 4°C. This fraction was mixed with leucoplatelet concentrate for enrichment with fibrinogen and other extracellular matrix proteins (fibronectine) and splitted into 8 small bags. In this way, it is possible to get topical hemocomponent that can be used for several applications with one autologous procedure. The leucoplatelet gel was made of autologous thrombin, cryoprecipitate-enriched platelet concentrate and gluconate of calcium. With this very cheap autologous procedure we succeed to reach a high cellular concentration without G-CSF patient stimulation, even if patient haematocrit was no more than 30%. The autologous procedure was well tolerated by patient and no side effects were observed.

Discussion

Platelet-rich plasma (PRP) method consists of collection and concentration of platelets (autologous or heterologous) that can release powerful growth-factors from their alpha and dense granules: PDGF, VEGF, TGFβ, FGF, EGF. All of them have the power to help tissue regeneration and cellular recruitment in the treated lesion. There are also the lipoxins, which are anti-inflammatory mediators [15-21]. This jel is an, antimicrobial, which can be used to fight against *E coli*, *Candida albicans*, MRSA and *Cryptococcus neoformans* [22]. PRP application can attract even the undifferentiated cells to the injury and promote angiogenesis and re-epithelialization [23]. PRP is t a potential remodel to fight the aged skin by using its ability to promote type I collagen formation and MMPs gene expression [24].

PRP method is also less expensive than single amount of isolated human factors. It is also minimally invasive, as it requires only small blood samples for each time [25]. Another advantage of using PRP instead of single amounts of human isolated growth factors is that PRP contains naturally balanced quantities of the growth factors, therefore it acts more likely to a physiological healing process [26-28].There are several systems to deliver PRP to the wound. Thrombin, $CaCl_2$, alginate beds, can be used for this purpose [29].

Our case report carries out the evidence that PRP therapy can improve the healing of pressure wounds even among debilitated patients as hematologic ones. By fastening the ulcers' healing process, this medication is improving the patients' conditions and their life quality.

Relavent review of literature and medical cases of skin ulcers treated with PRP are give in the Table 1. According to it, Scott et al. have showed in their case report [29] on how the right trochanter ulcer in a spinal cord injured patient that responded well to the PRP therapy with the development of tissue granulation, vascularization and epithelialization.

PRP can also successfully treat other kinds of ulcers, such as diabetic ones. This was demonstrated by Masoud Mehrannia et al. in the case of a diabetic patient with leg injuries [30]. Using PRP method, they managed to treat the wounds that were non responsive to traditional treatments. Dai Hyun Kim et al. [31] have achieved similar results by using PRP treatment on an old woman (94 year) who had a severe leg ulcer in a situation of various comorbidities. The lesion was not improving with daily simple dressings and periodic debridement. However, PRP could fill the granulation tissue and cure the wound in a span of two months.

Article and Authors	Number of Patients	Skin Wounds	PRP Treatment	Time of Treatment
Sell et al. A case report on the use of sustained release platelet-rich plasma for the treatment of chronic pressure ulcers [29].	3	3 pressure ulcers	autologous	Patient 1:8 weeks Patient 2:10 prp applications Patient 3:5 prp applications
Yuan et al. The preliminary application of autologous platelet-rich gel used to treat refractory diabetic dermal ulcer.	13	13 diabetic ulcers	autologous	69.2% cured in 3 weeks
Driver et al. A prospective, randomized, controlled trial of autologous platelet-rich plasma gel for the treatment of diabetic foot ulcers.	72 divided into two groups: 40 for prp treatment, 32 in a control group	40 diabetic ulcers	autologous	12 weeks
Sakata et al. A retrospective, longitudinal study to evaluate healing lower extremity wounds in patients with diabetes mellitus and ischemia using standard protocols of care and platelet-rich plasma gel in a Japanese wound care program.	39	24 ischemic diabetic, 10 diabetic, 5 ischemic, 1 pressure ulcers	autologous	83% in 145.2 days
Cervelli et al. Application of enhanced stromal vascular fraction and fat grafting mixed with PRP in post-traumatic lower extremity ulcers.	10	Post traumatic low extremity ulcers	Fat grafting + prp	97.8% in 9.7 weeks
Cervelli et al. Application of platelet-rich plasma in plastic surgery: clinical and in vitro evaluation.	18	Chronic lower extremity ulcers	Fat grafting + prp	88.9% in 9.7 weeks
Kim et al. Application of platelet-rich plasma accelerates the wound healing process in acute and chronic ulcers through rapid migration and upregulation of cyclin A and CDK4 in HaCaT cells.	16	11 chronic and 5 acute ulcers	autologous	9 of chronic ulcers healed in 15,18 days, the acute ones in 4-20 days

Sarvajnamurthy et al. Autologous platelet rich plasma in chronic venous ulcers: study of 17 cases.	12	17 venous ulcers	autologous	5.1 weeks
Martinez-Zapata et al. Autologous platelet-rich plasma for treating chronic wounds.	325	Chronic wounds	autologous	12 weeks (8 to 40)
Frykberg et al. Chronic wounds treated with a physiologically relevant concentration of platelet-rich plasma gel: a prospective case series.	49	65: the most common were 21 pressure, 16 venous and 14 diabetic ulcers.	autologous	97% improved in 2.8 weeks
De Angelis et al. Combined use of super-oxidised solution with negative pressure for the treatment of pressure ulcers: case report.	1	1 pressure ulcer	Intra- and per-lesional prp injections	Prp infections were followed by surgery, after which wound reduction was observed
Scimeca et al. Novel use of platelet-rich plasma to augment curative diabetic foot surgery [13].	1	Diabetic ulcer	autologous	7 weeks
Masoud Mehrannia et al. Platelet Rich Plasma for Treatment of Nonhealing Diabetic Foot Ulcers: A Case Report [30].	1	Diabetic ulcer	autologous	Treatment of 10 days, healed in 8 months
Knox et al. Platelet-rich plasma combined with skin substitute for chronic wound healing: a case report.	1	Decubitus ulcer	autologous	6 weeks
Saad Setta et al. Platelet-rich plasma versus platelet-poor plasma in the management of chronic diabetic foot ulcers: a comparative study.	12	Diabetic ulcers	Prp treatment efficacy was compared to platelet-poor plasma (ppp) control group	???
Kim et al. Recalcitrant cutaneous ulcer of comorbid patient treated with platelet rich plasma: a case report.	1	Traumatic cutaneous ulcer	autologous	7 applications of prp: healing in 3 months
Nishimoto et al. Supplementation of bone marrow aspirate-derived platelet-rich plasma for treating radiation-induced ulcer after cardiac fluoroscopic procedures: A preliminary report.	4	Radiation induced ulcers	Skin flap supplemented with autologous bone marrow prp	???
de Leon et al. The clinical relevance of treating chronic wounds with an enhanced near-physiological concentration of platelet-rich plasma gel.	200	285 chronic wounds	autologous	96.5% of wounds had positive results in 2.2 weeks
Dionyssiou et al. The effectiveness of intralesional injection of platelet-rich plasma in accelerating the healing of chronic ulcers: an experimental and clinical.	26	Chronic ulcers	surgical debridement and intralesional injection of PRP	10 healed in 7 weeks, 16 underwent on reconstructive procedure after woud bed preparation with prp
Cervelli et al. Tissue regeneration in loss of substance on the lower limbs through use of platelet-rich plasma, stem cells from adipose tissue, and hyaluronic acid.	30	Various chronic wounds	Autologous prp + fat grafts	100% improvement in 3 weeks, 47% healing in 6 weeks, 57% healing in 3 months
Sano et al. Treatment of chronic ulcer with elastic plasma protein and platelet film for wound dressing.	10	Chronic wounds	Plasma proteins + autologous prp: platelet-protein film	transcutaneous oxygen tension increased in 4 days, vascular density increased in 14 days.
Park et al. Treatment of refractory venous stasis ulcers with autologous platelet-rich plasma and light-emitting diodes: a pilot study.	16	Venous ulcers	Autologous prp + LED therapy	75% improved in 6 weeks
Salazar-Álvarez et al. Use of Platelet-Rich Plasma in the Healing of Chronic Ulcers of the Lower Extremity.	11	Non ischemic ulcers: venous and hypertensive ulcers	autologous	Improvement in 4 weeks

Table 1: Review of literature and medical cases of skin ulcers treated with PRP.

Conclusion

By applying PRP medications for a patient admitted at our hospital with non-Hodgkin linfoma, we succeed fully reduce the diameter of the pressure sore and to clear its bottom within 6 applications. This treatment ensured lower risk of infections and better quality of life for the patient which is very important for a patient in such a precarious condition.

PRP therapy improves and heals skin ulcers thanks to the combination of growth factors, anti-inflammatory mediators, antimicrobial effects and capacities to attract the undifferenciated cells

and to improve the angiogenesis and re-epithelialization. Its use can lead to far better results in healing skin ulcers of patients, including the hematologic ones. Faster healing, reduced hospitalization, easy and patient friendly treatment mechanism without surgery or amputations are the unique advantages of PRP method. It ensures quality of life for the patients while reducing the hospital costs considerably.

The study suggests that in order to understand the PRP applications in healing sking sores and wounds it is essential to take up larger studies with a representative sample.

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