Case Report

Application of Liquid Platelet-rich Fibrin for Treating Hyaluronic Acid-related Complications: A Case Report with 2 Years of Follow-up

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Abstract

Platelet-rich fibrin (PRF) is a blood concentrate system derived from the peripheral blood by means of centrifugation. In esthetic medicine, hyaluronic acid (HA) is safe and most frequently used for esthetic treatment and skin augmentation. However, some complications such as inflammation were reported in the literature after the injection of HA as a xenogeneic material. The present case report presents a case of the treatment of complication after HA injection. The subject received the injection of HA in combination with filler material and developed a purulent and granulomatous dermal and subdermal skin infection that was eliminated by incision. To prevent scar formation, the subject was treated with dermal and subdermal liquid PRF injections for 1 year, and the case was documented for 2 years. The PRF injections promoted wound healing and minimized the scar formation. After two sessions, the patient swelling and redness were significantly decreased compared to baseline. After 4 sessions, complete wound healing was achieved without obvious scar formation. This case report shows that the use of liquid PRF as a bioactive system promotes wound healing and skin regeneration as well as minimizes scar formation. However, controlled clinical studies are needed to further elucidate the benefit of PRF as an autologous and bioactive material for esthetic skin treatment.

Keywords: Lo- speed centrifugation concept, platelet-rich-fibrin, skin regeneration

Introduction

Over the last decade, the use of autologous blood concentrates has gained importance in different medical fields.[1] The main concept is based on the centrifugation of the peripheral blood to concentrate its components that are important for regeneration such as platelets, leukocytes, and plasma proteins.[2] Activated platelets release a series of growth factors (platelet-derived growth factors) that are involved in different cascades of angiogenesis, regeneration, and wound healing.[3] Blood concentrates, as reservoirs of growth factors, are widely used to promote wound healing and enhance regeneration in the bone and soft tissue.[4] The first generation of platelet concentrates, platelet-rich plasma (PRP), mainly includes platelets and plasma proteins. Its preparation procedure consists of two-step centrifugation and requires the addition of external anticoagulants. In addition, xenogeneic thrombin or calcium ions are added to PRP to activate platelets to release growth factors.[5] The use of external chemicals and activation factors may enhance the contamination risk and make the use of PRP in clinical routine an elaborate procedure. The further development of platelet concentrates led to the introduction of platelet-rich fibrin (PRF), which is a fully autologous system. PRF is obtained through one-step centrifugation without any anticoagulants.[6] In addition to fibrin, platelets, and plasma proteins, PRF includes a high number of leukocytes.[7] Depending on the blood collection tube and the centrifugation protocol, it is possible to generate either a solid or a liquid PRF matrix without anticoagulants. In terms of solid PRF, platelets interact with the glass surface of

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the tube and activate their coagulation during the centrifugation procedure.[2,6] Immediately after centrifugation, the resulting solid PRF matrix consists of a fibrin scaffold with entrapped platelets, leukocytes, plasma proteins, and growth factors. The liquid PRF is generated using a blood collection tube with a plastic surface that enables the generation of a liquid PRF matrix without the use of external anticoagulants. At room temperature, the resultant liquid PRF preserves its liquid condition for approximately 15–30 min and forms a fibrin clot thereafter.[8]

Extensive research aiming to understand the effects that centrifugation has on the components and bioactivity of PRF introduced the so-called low-speed centrifugation concept (LSCC).[2] This concept states that reducing the applied relative centrifugation force (RCF) during the centrifugation of PRF matrices significantly enhances the platelet and leukocyte number in the resultant PRF matrix. In addition, PRF matrices that are prepared using a low RCF release significantly higher concentrations of key growth factors such as vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), and platelet-derived growth factor (PDGF-BB), compared to matrices prepared with a high RCF.[2,8-10]

This case report presents the use of liquid PRF, prepared according to LSCC, for treating wound healing disorders, i.e., by a purulent and granulomatous dermal and subdermal skin infection associated with complications after hyaluronic acid (HA) treatment in the face for esthetic reasons.

Case Report

The subject is a 63-year-old otherwise healthy female who sought HA treatment for skin augmentation of the temporal head region and the periorbital regions. Two weeks after HA injection, a purulent and granulomatous dermal and subdermal skin infection occurred in both temporal regions of the head. The granulomatous parts were incised, and purulent tissue was emptied. This process was repeated for 6 weeks, with initial antibiotic therapy (Cefuroxime 500 mg; 1-0-1), which was confirmed by an antibiogram and continued for 2 weeks. The skin of the patient showed many signs of dermal and subdermal scars and visible skin defects due to the aforementioned therapy [Figure 1a and a']. Thereafter, liquid PRF was used to support wound healing and prevent further scar formation. The patient accepted the offered attempt of healing using liquid PRF as a minimally invasive treatment option and gave written informed consent for her treatment. In total, the patient received six treatment sessions. For each treatment session, 20 ml of peripheral blood (2 tubes of 10 ml; orange tubes PROCESS for PRF; NIS, France) was used for the PRF preparation as previously published.[2] The tubes were immediately placed in a preprogramed centrifuge with a fixed angle and a radius of 10 cm (DUO centrifuge, PROCESS for PRF, NIS, France) and were centrifuged according to a previously published protocol (600 rpm, 47 g, 8 min). After centrifugation, the liquid PRF was collected using a 5 cc syringe with 18-gauge × 2" needle [Figure 2a and b]. For each

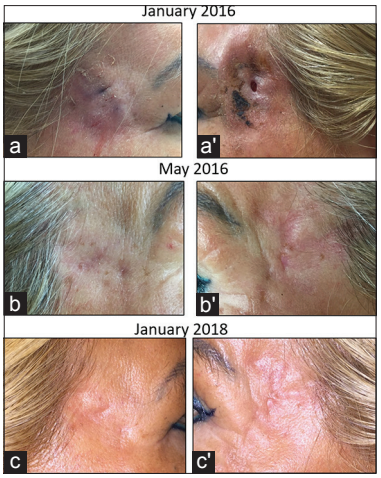

Figure 1: a-c Stages of wound healing and skin regeneration

temporal side, 2 ml of liquid PRF was injected subdermally using a syringe with a 25-gauge × 1.5" needle [Figure 2c], while 1 ml was used intradermally by a 30-gauge × 0.5" needle within the previously infected area [Figure 2d]. The treatment was repeated every 4 weeks until the wound completely healed and then every 3 months for 1 year. The case was documented at the 2-year follow-up.

After the second session with liquid PRF injection, the signs of inflammation, i.e., swelling and redness, were significantly decreased compared to baseline [Figure 1a and a']. According to the patient, the perceived pain was substantially reduced after the injection of liquid PRF. Subsequently, skin and soft-tissue regeneration associated with visibly reduced scars on both sides of the temporal region was achieved after 4 months, i.e., 4 injections. At this time point, the structure and color of the regenerated skin were already similar to those of the surrounding skin. The area of treatment had only a decedent superficial scar without obvious fibrous tissue [Figure 1b and b']. After 2 years, the patient endorsed total satisfaction with the esthetic and functional results based on her subjective evaluation of the treatment success [Figure 1c and c'].

Discussion

In esthetic medicine, different filler materials are used for superficial and deep soft-tissue augmentation.[11] Natural filling materials include collagen and HA. These materials are combined either with biologically degradable components such as poly-L-lactic as a resorbable material or with synthetic particles such as silicone or acrylates for long-term augmentation.[12] Further, HA is one of the most frequently used materials for soft-tissue augmentation in different regions of the face and head.[11] Its chemical structure, a polysaccharide consisting of D-glucuronic acid and D-N-acetylglucosamine disaccharide units, allows the polypeptide to bind to water and enhance skin hydration.[12,13] HA is mainly derived from animals or synthesized using bacteria to mimic the HA structure that naturally exists within the dermis.[14] The

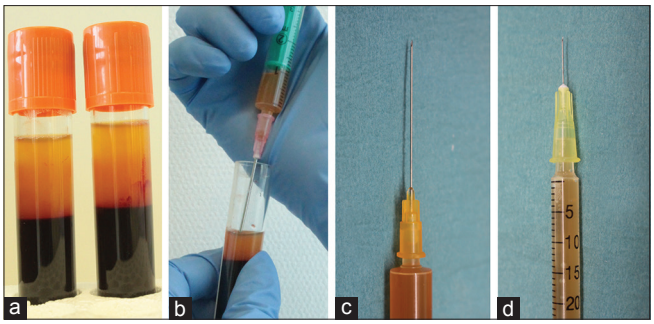

Figure 2: (a) Liquid PRF immediately after centrifugation. (b) Separation of liquid PRF from the red phase using a syringe and with a needle (18 gauge). (c) Syringe and needle (25 gauge) used for the intradermal injection. (d) Needle and syringe used for intradermal injection (30 gauge)

injection of HA is usually a safe procedure.[15] However, some local complications have been reported in the literature. In addition to inflammation and a possible allergic or immune response, skin necrosis due to vascular occlusion is the most serious complication following HA injection.[16] This case report presents a case of purulent granulomatous skin infection after injection of HA combined with silicone particles. This reaction may have occurred due to the impurity of the silicone particles or as a foreign body reaction in response to these particles. The classic treatment for this complication is a series of surgical interventions to remove the granulomatous area and allow wound healing, as performed in this patient before starting the PRF injection therapy. This invasive treatment is an additional burden for the patient and is accompanied by a risk of further wound healing dysfunction as a complication of each surgical treatment and of scar formation. The treatment option presented in this study (i.e., liquid PRF injection) is a minimally invasive alternative that includes a fully autologous system to regenerate the subdermal and dermal tissue. The here presented protocol of intervals was chosen to support the regeneration process during wound healing additionally to reduction of scar formation process. Therefore, in the first phase, PRF was injected every 4 weeks to allow a sufficient regeneration process. The re-application was used to boost the wound with the bioactive PRF components. After complete wound healing, PRF was used as a natural "filler" in terms of the included fibrin and a bioactive material to further reduce scar formation. In this case, the injection interval was set to every 3 months for 1 year.

Liquid PRF, which was prepared according to LSCC, is a concentrate of platelets, leukocytes, and their growth factors in a liquid fibrinogen-based matrix.[8] These components are greatly needed for wound healing. Recent studies have shown the capacity of liquid PRF to release high concentrations of PDGFs (PDGF-BB, PDGF-AB, and PDGF-AA), EGF, VEGF, and transforming growth factor-β1 over 10 days.[2,10,17] These growth factors are the main contributors to wound healing, especially in angiogenesis and epithelialization.[18,19] *In vitro* studies showed that the application of liquid PRF on human fibroblast significantly enhances their proliferation and activation.[20] In addition, the combination of liquid PRF with endothelial cells *in vitro* resulted in the formation of a significantly higher number of vessel-like structures compared to the untreated endothelial cells.[10] Moreover, an *in vivo* study showed that optimized PRF matrices prepared according to LSCC provide significantly higher vascularization than do PRF matrices that are prepared using a high RCF.[21] Therefore, liquid PRF can serve as an autologous source of growth factors that triggers cell-mediated vascularization and supports regeneration. However, no data were found on the use of liquid PRF in functional esthetic treatment. Therefore, this case report presents, for the first time, the use of liquid PRF for treating purulent granulomatous infections of the skin.

Physiological wound healing passes through three different phases: inflammation, proliferation, and regeneration.[22] Platelets, leukocytes, and their signaling molecules are the main contributors to the inflammation phase.[23] After these cells accumulate, they release signaling molecules to trigger additional cells involved in regeneration such as fibroblasts and endothelial cells.[23] However, the microenvironment in chronic wounds differs from physiologically healing wounds.[24] Chronic wounds primarily lack vascularization.[25] In the present case, the microenvironment of the wound healing disorder was influenced by injecting liquid PRF as a boost of cells and growth factors. This bioactive material (i.e., liquid PRF) may have led to changes in the inflammatory disequilibrium of the affected area and supported vascularization that led to healing and recovery. In addition, the release of EGF in liquid PRF supports the process of epithelialization, so wound closure is achieved without obvious scar formation or fibrosis.[26,27] A systematic review reported the use of solid PRF in plastic and reconstructive surgery. Four studies that included 116 patients used solid PRF as a wound dressing. Complete healing was achieved in 106 of the evaluated cases.[28] The use of this autologous system avoids the risk of an immune response or foreign body reactions. Our case report shows that this minimally invasive technique is a potential tool for esthetic medicine and skin regeneration. However, further controlled clinical studies are needed to elucidate the benefit of liquid PRF as an alternative material for different indications of skin regeneration.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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