CHAPTER 10

PLATLET GEL: A New Approach To Healing Diabetic Wounds

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Along with its illness, complications related to diabetes are becoming epidemic in the United States. One of the most significant complications of this devastating illness is non-traumatic lower limb amputation. Between 1997 and 1999 the non-traumatic lower limb amputation rate in diabetics was 82,000 each year.[1] According to Apelqvist and colleagues, the five-year mortality rate for diabetic patients is between 39-68% following a major amputation.[2,3] Further, it has been estimated by the National Center for Chronic Disease Prevention and Health Promotion that approximately 85% of these amputations could be prevented given adequate foot care programs that provide education and regular examinations.[3] Obviously, amputation patients, family members and health care providers suffer physical, financial and emotional losses related to diabetes and its complications. It is the purpose of this paper to introduce a new option for healing diabetic foot ulcers with the intent of offering better techniques in wound healing and decreasing the need for amputation. Autologous platelet gel tissue grafting is that option and will be discussed below.

Prevention and rapid healing of diabetic foot ulceration are major principles to avoiding amputation. Towards this end, each wound must be fully evaluated and managed with emphasis on both systemic factors as well as local wound factors. Systemically, the diabetic ulcer patient requires nutritional, medical, and diabetic management referrals and there are often indications for vascular and infectious disease consultations.

Wound debridement and offloading are important aspects of local healing, however, the challenge for diabetic wound healing specialists is often to select the appropriate supplemental wound treatment. In addition to hyperbaric oxygen therapy and subatmospheric (VAC) therapy, several topical preparations such as antimicrobials, debriding agents, absorbers, hydrators, living skin equivalents and growth factors are available for wound specific treatment.

Growth factor therapy has been recommended as a valuable adjunct in healing diabetic ulcers. The use of topical becaplermin gel .01% (recombinant platelet derived growth factor-BB) has demonstrated improved diabetic neuropathic ulcer healing in a randomized, prospective, double-blinded, placebo-controlled, multicenter 118 patient study.[4] In a 1990 prospectively randomized, blinded and placebo controlled 32 patient study, Knighton and colleagues applied a platelet releasate containing multiple growth factors to chronic, nonhealing, lower extremity wounds. Despite the problems with his small patient sample size, which was not randomized into diagnostic groups, and the fact that his patients were not equally distributed into treatment and control groups, the wounds in his study group patients did demonstrate a highly statistically significant improvement ($P<.0001$) in epithelialization.[5]

Several recent studies have demonstrated improved chronic wound healing with the use of single growth factors.[6-9] However, the only FDA approved topical recombinant growth factor treatment is becaplermin gel 0.01% and it is indicated only for diabetic foot ulcers. Consequently, there is one pharmaceutically available growth factor option available for the clinician. Autologous platelet gel tissue grafting offers several concentrated growth factors for the chronic wound. The procedure involves wound debridement and applying a growth factor rich platelet gel tissue graft to transform the chronic wound into an acute wound.

WHAT IS PLATELET GEL AND HOW IS IT APPLIED?

Autologous platelet gel (PG) is derived from the patient's platelet rich plasma (PRP). The initial step in generating this tissue graft is to remove up to one unit of the patients' blood by peripheral venous puncture. Using cell saver technology, whole blood is separated to isolate the platelet rich plasma. The PRP contains concentrated platelets, concentrated white blood cells, fibrinogen, cell adhesion molecules and a small proportion of red blood cells. When PRP is combined with thrombin and calcium chloride reagents both the soluble plasma protein fibrinogen and platelets are activated. Fibrinogen is converted into an insoluble fibrin gel which creates a mesh framework for platelet adhesion/aggregation, cell migration and for neo-vascular growth. Simultaneously, platelets are activated which initiates the coagulation

cascade, as well as, causing degranulation of its cytoplasmic alpha granules. The alpha granules of viable platelets contain several growth factors with varied wound healing functions (Table 1).[10-16]

The platelet rich clot (i.e., autologous platelet gel tissue graft) is applied directly to the wound after debridement has been performed. This semi-solid gel coagulum contains three to five times the normal platelet count of peripheral blood.[10,11] The release of platelet gel growth factors from platelet alpha granules offers high concentrations of growth factors to the chronic wound. These growth factors activate wound healing cells initially by binding to growth factor specific cell membrane receptors. Cell receptor binding stimulates an elaborate intracellular biochemical cascade resulting in gene transcription which ultimately effects tissue repair including cell replication, differentiation and chemotaxis.[12-16]

There are several clinical applications for platelet gels. One author stated that, "platelet gels have global applications in surgery".[12] To this date the efficacy of platelet gel for healing chronic diabetic wounds has been reported only by one author.[17]

Table 1

GROWTH FACTORS PRESENT IN PLATELET GEL

Platelet derived growth factor (PDGF)
-cell proliferation, chemotaxis, extracellular matrix production, angiogenesis

Transforming growth factor beta-1 and beta-2 (TGF B-1, TGF B-2)
-cell proliferation, differentiation and chemotaxis.
-matrix production:collagen, cartilage and bone

Epidermal Growth Factor (EGF)
-cell proliferation, chemotaxis
-angiogenesis, epithelialization

Insulin Like Growth Factor-1 (ILGF-1)
-cell proliferation, collagen synthesis
-angiogenesis

PROCEDURAL SPECIFICS

The procedure involves wound debridement and application of the platelet gel graft in the operating room (Figures 1-5). The margins of the wound are prepped with a skin adherent and the graft is held in place with a sterile occlusive dressing. A dry sterile dressing and elastic bandage are applied over the dressing. The patient is placed on postoperative oral antibiotics (e.g., cephalexin 500mg qid or clindamycin 300 mg tid if the patient has a penicillin allergy) for seven days and is instructed to be completely nonweightbearing. Hemoglobin, hematocrit and platelet counts are the only required preoperative labs for patients not receiving systemic anesthesia. The respective recommended lab values for this procedure are 10.0, 30.0 and 100. If smaller volumes of blood are drawn lower lab values may be acceptable.

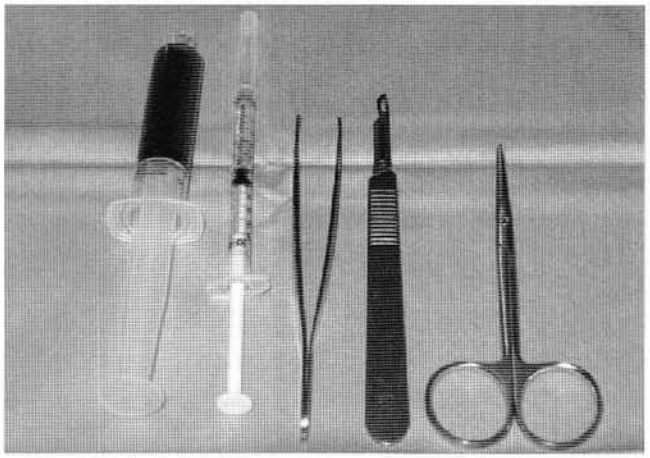

Figure 1. Instrumentation for platelet gel application. 10 cc platelet rich plasma (PRP), 0.5 cc thrombin and calcium chloride mixture and debridement instrumentation.

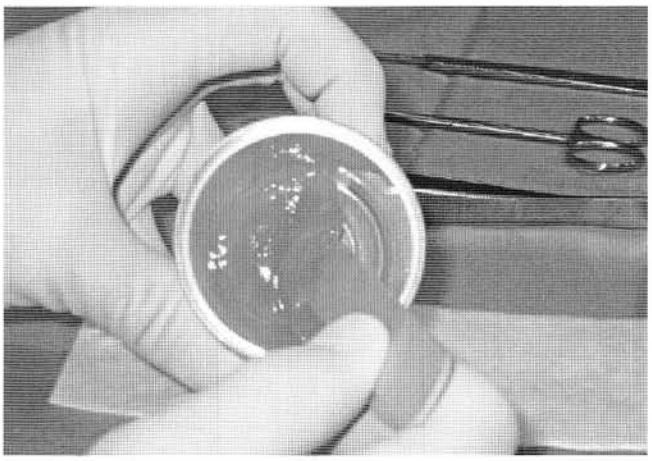

Figure 2A. Growth factor rich platelet gel clot formed by combining PRP, thrombin and calcium chloride.

The patient's wound is re-evaluated 5 days later and the dressing is completely removed but the wound bed is not disturbed. A hydrocolloid dressing (e.g., Duoderm CGF) is applied in the office and this dressing is changed every three to four days by the patient or home health nurse. If the wound is stable, the patient is seen every two weeks for debridement and re-evaluation. Systemic management and wound offloading is required throughout the duration of the wound healing process. Occasionally, the wound may require a second graft based on the progress of the wound.

CONCLUSIONS

Chronic wounds have demonstrated and increased level of growth factor degrading proteases.[18-21] The parity of growth factors in chronic wounds may be overcome by topically applying these biochemical messengers.[20-22] A new approach to the diabetic wound, autologous platelet gel tissue grafting offers several growth factors in their natural proportions and high concentration to encourage faster healing of the chronic wound. While controlled studies are needed to define the ideal protocol and patient selection criteria, this new procedure is extremely advantageous in that it offers readily available growth factors, the growth factors are available at a low cost, it is a relatively simple procedure, and it is a very low risk treatment for the patient.

Overall, it is this author's experience thus far, that platelet gel grafting demands that a team approach has been initiated for four weeks prior to performing this procedure. Specifically, this warrants that all basic primary approaches to wound healing have been systematically applied for one month, including podiatry,

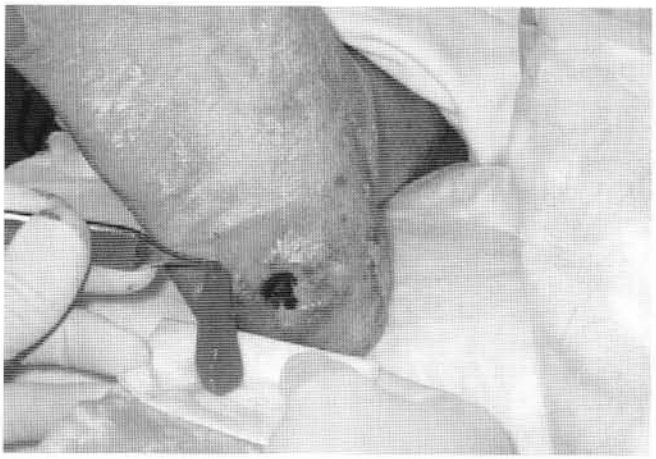

Figure 2B. Gel consistency provides flexibility for manipulating graft to wound dimensions.

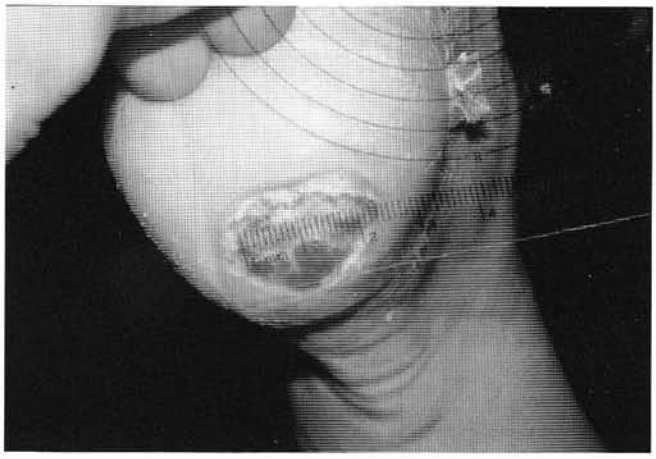

Figure 3. Decubitus right foot heel ulcer in a 68 year old diabetic patient. This ulcer developed during convalescence following a left below knee (BK) amputation and had been present for 247 days. Pedal pulses were non palpable and the patient was not a lower extremity vascular bypass candidate.

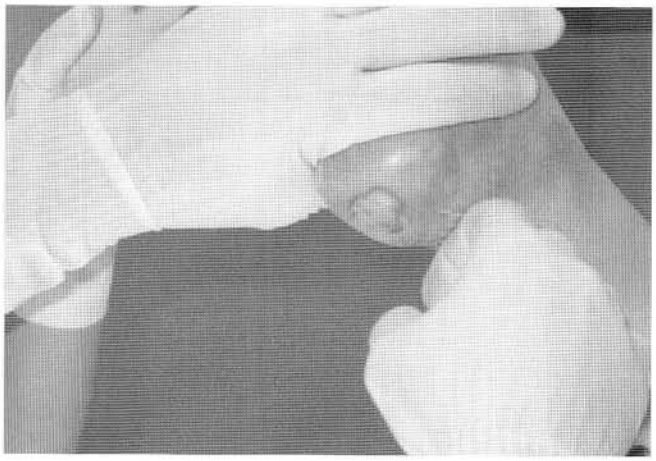

Figure 4. Sterile Tegaderm holding platelet gel graft in place. This dressing was removed after five days and the patient was kept nonweightbearing during the postoperative period. Wound care consisted of debridement every 2-3 weeks and Duoderm CGF dressings applied every four days.

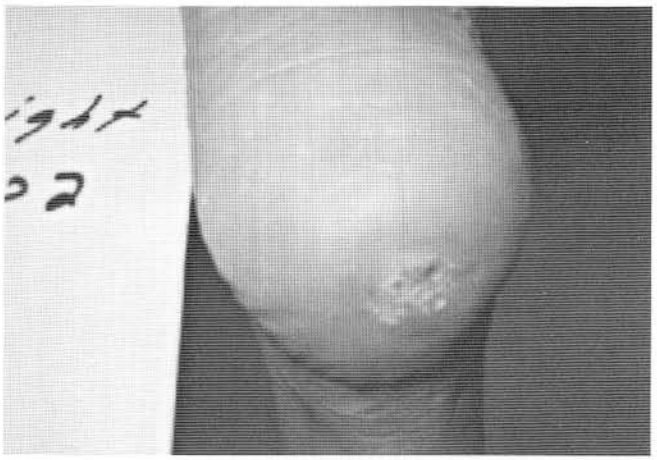

Figure 5. The ulcer is healed 82 days after autologous platlet gel grafting. The patient remains ulcer free and is ambulating with a BK prosthesis on her left side at this writing 4 months after healing.

internal medicine/endocrinology, nutrition, vascular and infectious disease. Platelet gel grafting is a significantly preferred approach for treating chronic diabetic wounds that inevitably seem to lead to amputation only after all other primary wound care approaches have been initiated. Because platelet gel grafting is not indicated for infected and ischemic wounds, it is not a panacea. It does however provide optimism for the refractory wound.

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