Enhanced Clinical Effects of Combining Recombinant PDGF with Collagen Dressings in Difficult to Heal Chronic Wounds

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BACKGROUND: It is well established that growth factors, their cellular receptor proteins, and extracellular matrix (ECM) proteins play key roles in promoting normal wound healing. Multiple clinical studies have established that chronic wounds with elevated protease activities (EPA) do not heal well, presumably due in large part to proteolytic destruction of growth factors (GF) that are essential for healing.[1,2,3] This led to the development of a topical preparation of recombinant human platelet derived growth factor (rhPDGF1) that is approved for treatment of lower extremity diabetic neuropathic ulcers that extend into the subcutaneous tissue or beyond and have an adequate blood supply. In addition to frequent debridement, which presumably reduces EPA,[4] combining rhPDGF with collagen dressings has been reported in case series over the years[5,6] to enhance its clinical effect, presumably by protecting the rhPDGF from proteolytic destruction through reversible binding and then re-release as the collagen matrix biodegrades, Additionally, some dressings provide a dermal template that enhances migration of wound cells into the wound bed.

PATIENTS STUDIED: We have utilized this combination for the past 12 years on chronic wounds that have either been slow to progress or as an initial treatment for patients who will be predictably difficult to heal due to co-morbid conditions or past wound history. Eight representative patient cases are presented with their key clinical data from the past 12 years that utilized this combination therapy of rhPDGF and collagen containing dressings.

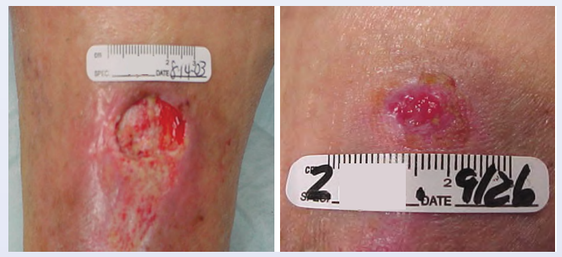
RESULTS: The chronic wounds in these representative 8 cases showed remarkable improvement with robust granulation tissue, and in 7 of them covering exposed bone, tendon or fascia in a relatively short period of time.

CONCLUSIONS: While there are an ever growing number of advanced cellular and tissue products available, there are reimbursement challenges with bundling of services and procedures, differences in reimbursement based on payer source, wait times until more advanced products can be utilized as well as often high co-pays for the patients. Utilizing this combination as soon as the wound is prepared can take the wound to closure in some cases, but also provide for an improved wound bed for better results with the advanced products.

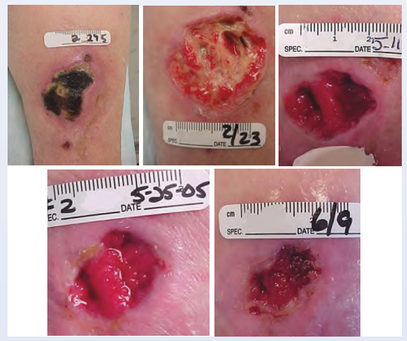
1. Ladwig G, Robson M, Liu R, Kuhn M, Muir D, Schultz GS. Ratios of activated matrix metallopro-teinase-9 to tissue inhibitor of matrix metallopro-teinase-1 in wound fluids are inversely correlated with healing of pressure ulcers. *Wound Repair Regen*. 2002 Jan-Feb;10(1):26-37
2. Lobmann R, Schultz G, Lehnert H. Proteases and the diabetic foot syndrome: mechanisms and thera-peutic implications. *Diabetes Care*. 2005 Feb;28(2):461-71
3. Snyder R, Driver V, Fife C, Lantis J, Peirce B, Serena T, Weir D. Using a diagnostic tool to identify elevated protease activity levels in chronic and stalled wounds: a consensus panel discussion. *Ostomy Wound Manage*. 2011 Dec;57(12):36-46
4. Steed DL, Donohoe D, Webster MW, Lindsley L. Effect of extensive debridement and treatment on the healing of diabetic foot ulcers. *Diabetic Ulcer Study Group*. J Am Coll Surg. 1996 Jul;183(1):61-4
5. Carson S, Travis E, Overall K, Lee-Jahshan S. Using Becaplermin Gel with Collagen Products to Potentiate Healing in Chronic Leg Wounds. *Wounds*. 2003;15(10).
6. Hollister C, Li V. Using Angiogenesis in Chronic Wound Care with Becaplermin and Oxidized Regenerated Cellulose/Collagen. Nursing Clinics of North America 42; 457-465. Elsevier Saunders 2007.

- 43 year old male, excellent health
- Sheriff's deputy
- Leg impaled on lake dock
- Wound infection w/ debridement
- NPWT with ultimate tibial exposure
- PDGF[1] gel applied over exposed bone
- SIS[2] matrix placed over PDGF, covered with oil emulsion contact layer
- NPWT continued
- Granulation tissue over bone in 10 days

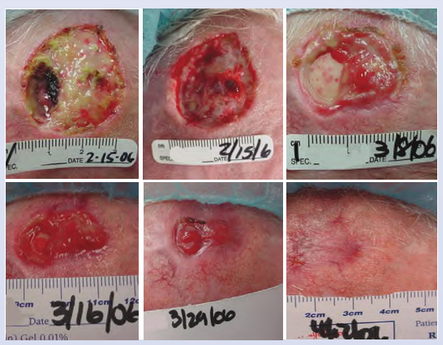
- 42 year old sheriff's deputy
- Dog bite to calf, no initial medical treatment with subsequent infection; sent for debridement
- Fascia exposed, began NPWT
- PDGF[1] gel and SIS[2] matrix added 5 days later
- PDGF[1] gel and SIS[2] matrix added 5 days later (7/26)
- NPWT continued
- Fully granulated in one month



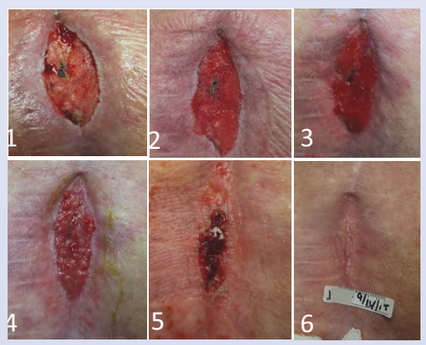
- 54 year old female
- PMH unremarkable other than venous insuffi-ciency with previous ulcers
- Works retail at local theme park
- Dehiscence of surgical incision at site of previous ulcer with further skin damage due to CVI
- Post debridement down to fascia
- Multi-layer wrap for management of edema
- SIS[2] matrix moistened with PDGF[1] gel applied weekly
- Results at week 6



- 84 y/o female
- History of CAD and cardiomyopathy
- Showered emboli to extremities
- Debrided sharply and with papain-urea ointment
- Slow to granulate over next 3 months



- 77 year old male
- S/P Mohs surgery for SCC of forehead; wound necrosed
- Ultrasonic debridement in clinic
- Skull exposed once free of necrotic tissue
- Began ORC/Collagen/AG[4] and PDGF[1] gel
- 8 days later rapid granulation over bone
- Closed over next 2 weeks



- 57 year old male s/p CABG with dehisced sternal wound
- Had used NPWT for 10 days prior to first visit
- Scattered bone exposed / palpable (photo 1)
- Day 14 added PDGF1 Gel and Ovine Collagen Dermal Template5 dressing (photo 2)
- Day 21 bone granulated over. NPWT discontinued, continued PDGF[1] Gel and Dermal Template[5], cov-ered with pigmented antimicrobial foam[6] (photo 3)
- Healing continued (photos 4-5), closed at Day 58 (photo 6)

- 68 year old Hispanic female, type 2 diabetes (poorly controlled), smoker, HTN, venous insuffi-ciency, lower extremity ulcer almost circumferential around leg, adequate blood flow
- Poor historian, two months into care obtained in-formation of history of pathergy, presumed dx of pyoderma gangrenosum. Treated medically.
- Utilized multilayer wraps for edema management, collagenase[7] and pigmented foam[7] (changed weekly) to achieve debridement. Once debrided tendon exposed medial calf (7/15/15)
- Began PDGF[1] gel and Ovine Collagen Dermal Template[5] 8/10/15 w/MLW[8]
- 10/12/15 Bridged into two smaller ulcers

- 30 y/o Hispanic male, type 2 diabetes, developed abscess to dorsal foot w/debridement. Discharged w/NPWT but poorly tolerated and removed. Ab-sorptive products used with compression wrap.
- 6/19/15 began PDGF[1] gel with ORC/Collagen[4] and contact layer protecting tendons, changed 2X week under MLW
- 6/30/15 tendons covered with granulation tissue
- 7/14/15 changed to PDGF[1] gel with Ovine Colla-gen Dermal Template[5] changed weekly with MLW
- 7/23/15 wound bridged in center
- 8/31/15 wound essentially closed.

Legend for products: 1. Regranex® (becaplermin) 0.01% Gel; 2. OASIS® Wound Matrix; 3. Promogran® Dressing; 4. Promogran Prisma® Dressing; 5. Endoform® Dermal Template Dressing; 6. Hydrofera® Blue Classic; 7. Collagenase – Santyl® Ointment; 8. MLW – Multilayer Wrap