

Clinical Course of Two Chronic Venous Leg Ulcers in a Sickle Cell Patient Treated with cfAF*: Divergent Healing Trajectories & the Impact of Infection

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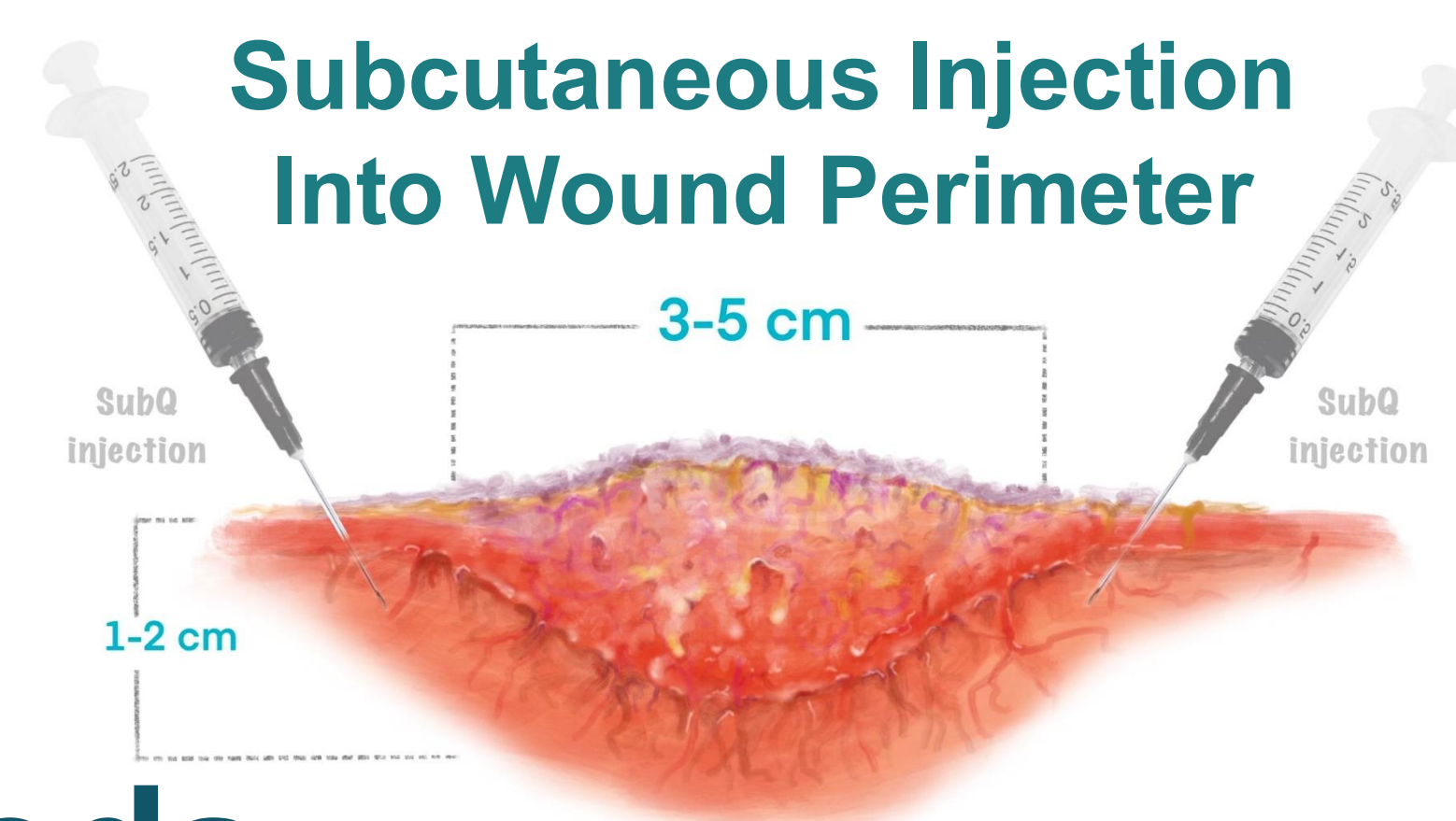
Introduction and Background

- Patients with sickle cell disease (SCD) often develop chronic lower-extremity ulcers that are prone to complications and high recurrence.
- SCD ulcers exhibit increased protease activity that degrades extracellular matrix components and disrupts normal granulation and re-epithelialization, contributing to chronic nonhealing wounds.¹⁻³
- This case report describes differential healing outcomes of two venous leg ulcers (VLUs) in a patient with SCD receiving a cell-free amniotic fluid-derived injectable biologic therapy, cfAF*.

Clinical Rationale & Mechanism

- SCD ulcers are characterized by chronic inflammation, ischemia-reperfusion injury, and excessive protease activity that disrupts extracellular matrix integrity and delays wound closure.
- cfAF* is an investigational drug containing protease inhibitors and exosomes for wound margin injection therapy (Figure 1) and represents a novel approach to target elevated proteases and activate healing pathways.

Figure 1. cfAF* Application Methodology.



Methods

- A 38-year-old black female with SCD and two VLUs: a 4-month-old left lateral ankle ulcer (Wound #1) and a 1-week-old left medial ankle ulcer (Wound #2). Failed prior treatments including both amniotic and synthetic grafts, collagen, antimicrobial foam, and compression.
- Wound #1 exudate was collected by swab at Baseline and Week 4.
- Wound #1 was treated over 31 weeks with twelve (12) peri-wound margin injections ranging from 0.5 to 1.0 mL, with local anesthetic.
- Wound #2 was treated over 31 weeks with seven (7) peri-wound margin injections ranging from 0.2 to 1.5 mL, with local anesthetic.
- Debridement was performed and amnion was applied at 4 visits for Wound #1 and 3 visits for Wound #2.
- Wound area, percent area reduction (PAR), pain, debridement, dressing, and adverse events were documented.
- Fluorescence resonance energy transfer (FRET) assays were used to evaluate host protease activity – including human neutrophil elastase (HNE) and matrix metalloproteinases (MMPs) – as well as bacterial protease activity.

Results

- **Wound #1 (Figure 2):** Area decreased from 6.3 cm² to 0.1 cm² (98.4% PAR) over 31 weeks (Figure 3). Granulation tissue was consistently present. Pain remained VAS 0 except brief spikes (VAS 9–10) during a moderate surrounding skin AE, assessed as unrelated to cfAF*.
- **Wound #2 (Figure 2):** Initial closure by Week 5 but subsequently reopened. Staphylococcus aureus infection at Week 12 (unrelated to cfAF*) drove wound area expansion from 0.6 cm² to 18.4 cm² (–2967% PAR) over 31 weeks (Figure 3); with VAS 9-10 pain during infection.
- **Protease Activity (Table 1):** Baseline FRET analysis demonstrated elevated host proteases (HNE: 10,953 µg; MMPs: 54,817 µg) and bacterial proteases (31,413 µg) in Wound #1 exudate. By Week 4, HNE and MMPs were undetectable, while bacterial proteases had decreased >99% to 83 µg.

Figure 2. Photography, Wounds #1 and #2.

Wound 1 - Left Lateral



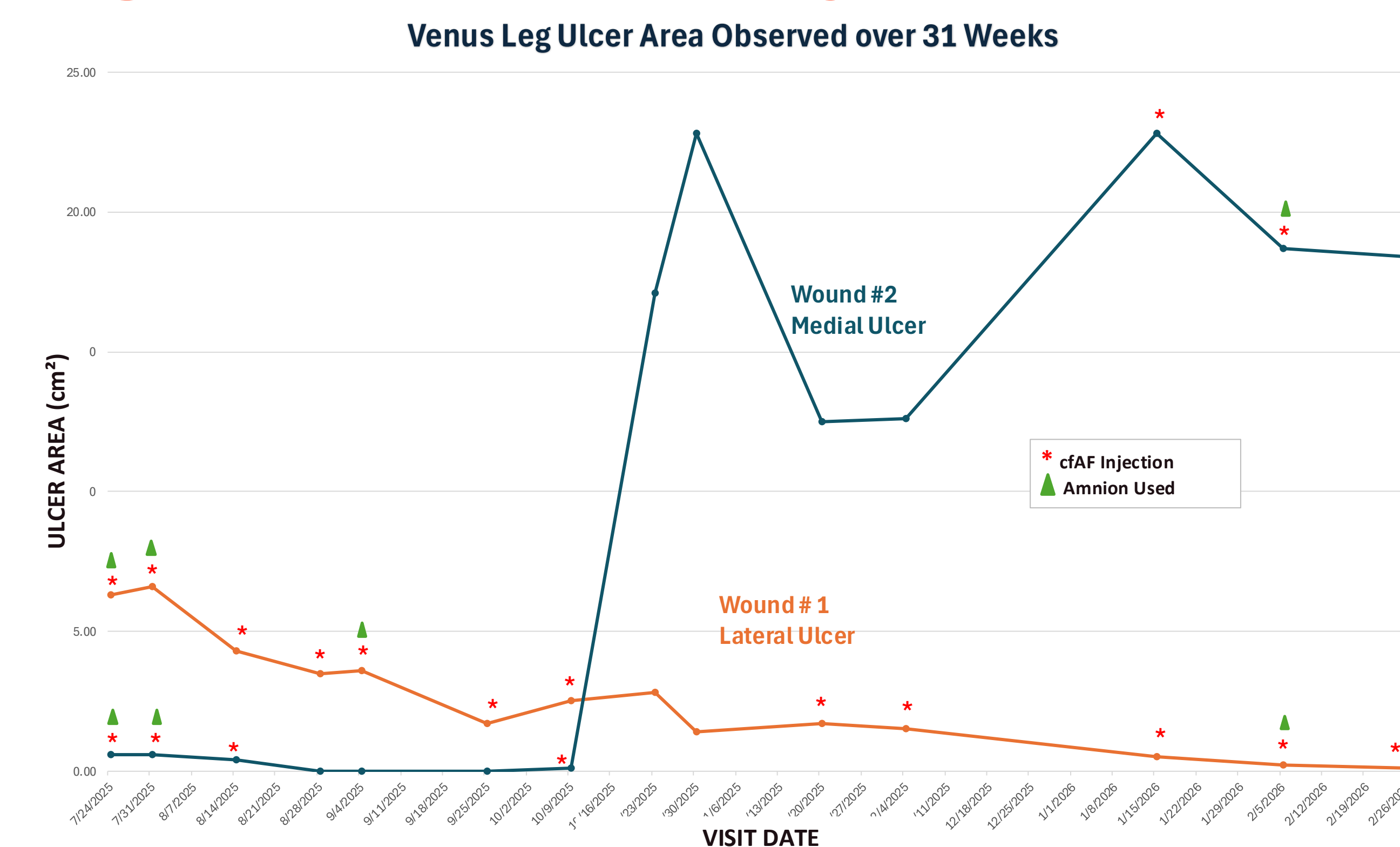
Wound 2 - Left Medial



Table 1. Wound #1 Protease Activity by FRET.

Measurement Time	Matrix Metalloprotease (ug)	Human Neutrophil Elastase (ug)	Bacterial Protease (ug)
Baseline	54,917	10,953	31,413
Week-4	0	0	83

Figure 3. Wound Area by Visit Date.



Conclusions

- **Healing response:** The chronic lateral ulcer achieved 98.4% area reduction over 31 weeks with sustained granulation and minimal pain following peri-wound cfAF injections.
- **Biologic signal observed:** Host proteases (HNE, MMPs) declined from markedly elevated levels to undetectable by Week 4, while bacterial proteases decreased >99%, consistent with restoration of a pro-healing wound environment.
- **Infection alters outcomes:** A Staphylococcus aureus infection disrupted healing in the medial ulcer after initial closure, underscoring infection control as critical determinant of therapeutic outcomes in SCD ulcers.

References

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Declaration of Interests

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