



Case Report

First Case of Accelerated Healing of a Recalcitrant Diabetic Ulcer Using Purified Amniotic Fluid

Pascal J Goldschmidt-Clermont*, Ian A White

Neobiosis LLC, UF Sid Martin Innovate Biotechnology Institute, Alachua, FL 32615, USA

***Corresponding author:** Pascal J Goldschmidt-Clermont, Neobiosis LLC, UF Sid Martin Innovate Biotechnology Institute, Alachua, FL 32615, USA

Citation: Goldschmidt-Clermont PJ, White IA (2023) First Case of Accelerated Healing of a Recalcitrant Diabetic Ulcer Using Purified Amniotic Fluid. Ann Case Report. 8: 1463. DOI:10.29011/2574-7754.101463

Received: 26 September 2023, **Accepted:** 29 September 2023, **Published:** 02 October 2023

Abstract

We report the first case of recalcitrant diabetic wound treated successfully by twice-daily applications of a sterile fraction of human purified amniotic fluid (ViX001) obtained from thoroughly screened volunteers at the time of planned c-section at the term of normal pregnancies. Our product ViX001 was generated through a proprietary process and kept in frozen one milliliter (1 ml) vials (protein content was ~1mg/ml) thawed prior to applications (shelf life at 34oF of at least two weeks).

Keywords: Purified Amniotic Fluid; Diabetic Wound; Diabetic Foot Ulcer; Extracellular Vesicles; Exosomes; Inflammation; Pain; Wound Healing; Tissue Repair, Regenerative Medicine, Neo-angiogenesis.

Introduction

Diabetic foot ulcer is a dreadful complication of diabetes, and often results in amputation of the foot. There are no cures for diabetic foot ulcers, and current treatments are usually protracted and of unpredictable effectiveness. Reports have suggested that extracellular vesicles (EV) produced by human umbilical cord mesenchymal stem cells (MSC) could improve angiogenesis and diabetic wound healing [1]. Similar findings were reported for EV from adipose tissues but not bone marrow MSC [2-4]. Scarless fetal wound healing is a known phenomenon [5], and the skin of the fetus is continuously exposed to amniotic fluid. Since amniotic fluid has evolved over more than 7,000,000 years for the human species [6], it is likely that it has evolved to maximally protect the fetus skin. Hence, we sought to study the impact of wound application of ViX001 on a diabetic wound that was resistant to standard treatment (recalcitrant).

Case Presentation

Our patient is a man in his late 70's with a history of type-2 diabetes mellitus that was discovered in his mid-60's when he

presented with an infected wound that was challenging to heal. In August 2022, he had contracted a new ulcer centered on the left Achilles heel while in the ICU following a pulseless arrest from which he was successfully resuscitated. His diabetes was treated according to state-of-the-art, except for GLP-1 agonists that the patient did not tolerate due to side effects. The wound was painful when moving his foot up and down (6/10), and deep enough to display the calcaneal tendon. It was debrided and treated for five months at the wound clinic of his health system with a combination of systemic antibiotics and two creams: Coloplast Triad Hydrophilic Wound Dressing and Mupirocin 2% Topical Ointment. A vascular surgeon confirmed that there was sufficient blood flow to his left foot, but the ulcer did not heal at all over the five months. Then at the beginning of January 2023, after signing an informed consent, the patient and his family decided to try a new treatment consisting of applications twice daily (AM and PM) of a drop (0.05 ml) of ViX001 on top of the wound concavity that was left unperturbed for 15 minutes then covered by a standard Band-Aid. Immediately after the first application, the pain and inflammation resolved and never returned. Wound healing was detectable through a concentric process of tissue growth (Figure 1) which progressively filled the ulcer. At the end of the healing, it became difficult to apply 0.05 ml of ViX001, as the concavity of the ulcer had been filled by new tissue, only a 0.01 ml drop could be retained by then. After 60 days, ViX001 applications were

discontinued, and the healed wound was covered instead with sterile White Petrolatum (Dynarex). The new skin remained intact for the next three weeks of follow up, and is still intact six months after treatment discontinuation. No adverse reactions, allergic, infectious or else, were recorded throughout the sixty days of treatment and six months follow up period.

Figure 1:



Figure 1: Evolution of the diabetic ulcer of the patient with twice daily applications of a sterile fraction of human purified amniotic fluid (hPAF) ViX001. The left picture shows the wound after 4.5 months of standard treatment (December 15, 2022). The next picture is on the day of the first application of HPAF (January 8, 2023). Picture 7 from the left is the day of the last ViX001 treatment (March 8, 2023), and the next two pictures are after two weeks and 6.5 months of follow-up, respectively. Note the immediate impact of ViX001 on inflammation of surrounding tissues and the progressive filling of the ulcer with new healthy skin tissue.

Discussion

We have previously reported skin regeneration induced by ViX001 in a 24-year-old woman who had suffered from full-thickness burns to her legs resulting from a rogue firework [7]. Pain dropped from 10/10 to 2/10 within an hour of application. With this report, we confirm that ViX001 has an immediate impact on wound pain and inflammation surrounding the wound. We purposefully selected a relatively small wound (13 millimeters) to test our hypothesis that ViX001 could accelerate diabetic wound healing. The wound of our patient was not healing at all with standard therapy in the prior five months and had the potential to compromise the Achilles heel tendon and to trigger infectious complications. Based on the success of this first case, we are now preparing a phase 1/2 study with a larger cohort of type-2 diabetic patients and with a greater variety of wound sizes. We also plan to explore the mechanism responsible for the accelerated healing of the diabetic wound, our preliminary data suggest that the extracellular vesicles (~150 nm in diameter) of the ViX001 and their content are primarily responsible for the anti-inflammatory and pro-angiogenic impact effects of our product on the reconstruction of injured tissues [8,9]. This case supports the further exploration of the use of products refined by nature over millions of years as potential solutions for the healing of complex skin wounds [10-12].

Acknowledgment: The authors want to thank the patient and his family for their invaluable support all along this study.

References

1. Jiang M, Jiang X, Li H, Zhang C, Zhang Z, et al (2023) The role of mesenchymal stem cell-derived EVs in diabetic wound healing. *Front Immunol*. 14:1136098.
2. Pomatto M, Gai C, Negro F, Cedrino M, Grange C, et al (2021) Differential therapeutic effect of extracellular vesicles derived by bone marrow and adipose mesenchymal stem cells on wound wealing of diabetic ulcers and correlation to their cargoes. *Int J Mol Sci*. 22:3851.
3. Deng H, Chen Y (2022) The role of adipose-derived stem cells-derived extracellular vesicles in the treatment of diabetic foot ulcer: Trends and prospects. *Front Endocrinol (Lausanne)*. 13:902130.
4. Jiang M, Jiang X, Li H, Zhang C, Zhang Z, Wu C, Zhang J, Hu J and Zhang J (2023) The role of mesenchymal stem cell- derived EVs in diabetic wound healing. *Front. Immunol*. 14:1136098.
5. Larson BJ, Longaker MT, Lorenz HP (2010) Scarless fetal wound healing: a basic science review. *Plast Reconstr Surg*. 126:1172-1180.
6. Goldschmidt-Clermont PJ, Hubinont C, Goldschmidt AJP, DiFede DL, White IA (2021) Pregnancy, a unique case of heterochronic parabiosis and peripartum cardiomyopathy. *Front Biosci (Landmark Ed)*. 26:666-672.
7. Kweh, MF, Parks M, Salerno A, Vaughn NE, White IA (2023) Topical Application of Purified Amniotic Fluid Accelerated Healing of Full-Thickness Burns, Negating the Need for Skin Grafts: A Case Report. *Journal of Wound Management and Research* 19: 53-58.
8. Underwood, M., Gilbert, W. & Sherman, M (2005) Amniotic Fluid: Not Just Fetal Urine Anymore. *J Perinatol* 25: 341-348.
9. Zhang Y, Yan J, Liu Y, Chen Z, Li X, et al (2021) Human Amniotic Fluid Stem Cell-Derived Exosomes as a Novel Cell-Free Therapy for Cutaneous Regeneration. *Front. Cell Dev. Biol*. 9:685873.

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10. Fukutake M, Ochiai D, Masuda H, Abe Y, Sato Y, et al. (2019). Human amniotic fluid stem cells have a unique potential to accelerate cutaneous wound healing with reduced fibrotic scarring like a fetus. *Hum. Cell* 32: 51–63.
11. Balbi C, Piccoli M, Barile L, Papait A, Armirotti A, et al (2017) First characterization of human amniotic fluid stem cell extracellular vesicles as a powerful paracrine tool endowed with regenerative potential. *Stem Cells Transl. Med.* 6: 1340–1355.
12. Huh MI., Kim MS., Kim HK. et al (2014) Effect of conditioned media collected from human amniotic fluid-derived stem cells (hAFSCs) on skin regeneration and photo-aging. *Tissue Eng Regen Med* 11: 171–177.