Innovative treatment of diabetic ulcers: combining chemical debridement and xenograft applications: a case study

Abstract: Lower extremity diabetic ulcers (LEDUs) are a common, high-morbidity complication of diabetes, frequently leading to infections, hospitalisations and emergency department visits. This case study examines the treatment effectiveness of a novel wound care approach in a 57-year-old female patient with a hard-to-heal LEDU (a diabetic foot ulcer of the left lower extremity) complicated by poorly controlled diabetes (glycated haemoglobin A1c: 13%). Initially, standard of care (SoC) practices, including alginate dressings, hypochlorous acid gel and sharp debridement, were ineffective in promoting significant healing. This case was further challenged by its occurrence in the remote setting of Tongatopu within the Kingdom of Tonga, where advanced wound care materials and even SoC products are not consistently available, underscoring the need for innovative and adaptable treatment strategies. A new regimen was subsequently initiated that involved preparing the wound bed through chemical debridement using a topical desiccating agent (TDA) with methanesulfonic acid (DEBRICHEM, DEBx Medical, the Netherlands), which has the ability to denature proteins and reduce microbial biofilms, necrotic tissue and inflammatory proteins in the wound bed. This was followed by the application of ovine forestomach matrix (OFM) grafts containing hyaluronic acid (Symphony, Aroa Biosurgery, New Zealand), which was applied at approximately 12-day intervals. Over the 110 days following the initial application of the TDA, the LEDU showed significant improvement as it progressed along the healing cascade towards closure. This case report provides insights into the potential of combined desiccating chemical debridement and xenograft-based wound care in treating hard-to-heal LEDUs, highlighting an approach that could inform future clinical practices in diabetic wound care.

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chemical debridement • diabetes • diabetic ulcer • hyaluronic acid • lower extremity diabetic ulcer • ovine forestomach matrix • topical dessicating agent • ulcer • wound • wound care • wound dressing • wound healing • xenografts

According to data, approximately 10.5% of the global population was affected by diabetes in 2021, with estimates placing the number of people living with diabetes at over half a billion worldwide.[1] In the US, the economic burden of diabetes amounted to $327 billion USD in 2017, which included $90 billion USD in reduced productivity.[2] Affecting about three million patients annually in the US, lower extremity diabetic ulcers (LEDUs) account for $0.6–4.5 billion USD in Medicare costs, increasing to $6.0–18.7 billion USD when factoring in complicating infection management.[3]

LEDUs are not only costly but also pose significant risks to patient health. These ulcers are a common, high-morbidity complication of diabetes, frequently leading to infections, hospitalisations and emergency department visits.[4,5] Over half of LEDUs develop infections, often progressing to osteomyelitis, and up to 20% of infected LEDUs require major or minor amputations.[3] The longer an LEDU remains open, the greater the risk for complications, including infection, osteomyelitis and amputation.[6] In patients with diabetes, 85% of lower-extremity amputations are preceded by a non-healing LEDU, with an estimated 49–85% of these amputations being preventable.[7,8]

Traditional management strategies, including routine dressings, debridement and the use of antimicrobial agents, often fail to promote wound closure, particularly in the presence of underlying diabetic conditions.[9] This report explores a novel intervention combining a topical desiccating agent (TDA) with methanesulfonic acid (DEBRICHEM, DEBx Medical, the Netherlands) and ovine forestomach matrix (OFM) xenografts containing hyaluronic acid (Symphony, Aroa Biosurgery, New Zealand).[10] These were applied in a clinical setting to treat a hard-to-heal LEDU in a patient with poorly managed diabetes. By detailing the methods and outcomes of this treatment, this case report aims to provide a model for alternative LEDU management that may improve patient outcomes in similar cases.

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Patient consent

The patient gave verbal approval and signed an informed consent form allowing the publication of her case and to use her images.

Case report

A 57-year-old female patient with a hard-to-heal LEDU (a diabetic foot ulcer (DFU) of the left lower extremity) complicated by poorly controlled diabetes (glycated haemoglobin A1c: 13%) was seen in an outpatient diabetic wound care clinic at the Vaiola Hospital in the Kingdom of Tonga. The patient's LEDU was initially treated with standard of care (SoC) procedures, including alginate dressings, hypochlorous acid gel and selective sharp debridement, and provided with an offloading walking boot, over 38 days, which resulted in no significant improvement. A TDA was applied to the wound base to reduce bioburden through its rapid desiccating properties (Fig 1), producing a characteristic caramelised, desiccated appearance upon removal (Fig 2). An ankle-brachial pressure index showed non-compressible vessels; however, with no endovascular or surgical revascularisation options available to the patient, no further vascular studies were possible.

Several days after applying the TDA, the patient's course was further complicated by a pressure injury from dress shoes that she had worn to church. When the patient returned to the clinic, surgical debridement was required to remove the necrotic tissue, along with the implementation of more aggressive offloading measures and patient wound care re-education. Following the debridement, an OFM graft enriched with hyaluronic acid was applied (Fig 3). The OFM was hydrated with a stabilised hypochlorous acid solution (Puracyn, Innovacyn, Realto, US) then covered with a bordered foam dressing. Offloading via a walking boot was continued. Over the next two months, five graft applications were performed approximately every 12 days. Wound area measurements and assessments were recorded at each treatment stage to evaluate healing progression.

Results of treatment

The combination treatment yielded a marked improvement in wound healing. At follow-up three months later, the left LEDU had reduced in surface area by 88% (Fig 4a). Within 110 days from the initial chemical debridement with the TDA, the LEDU area had closed (Fig 4b). The application of the OFM graft facilitated progressive wound closure, showcasing the effectiveness of combining biofilm-reducing debridement with hyaluronic acid-enriched OFM grafts in managing LEDUs resistant to SoC techniques alone.

Discussion

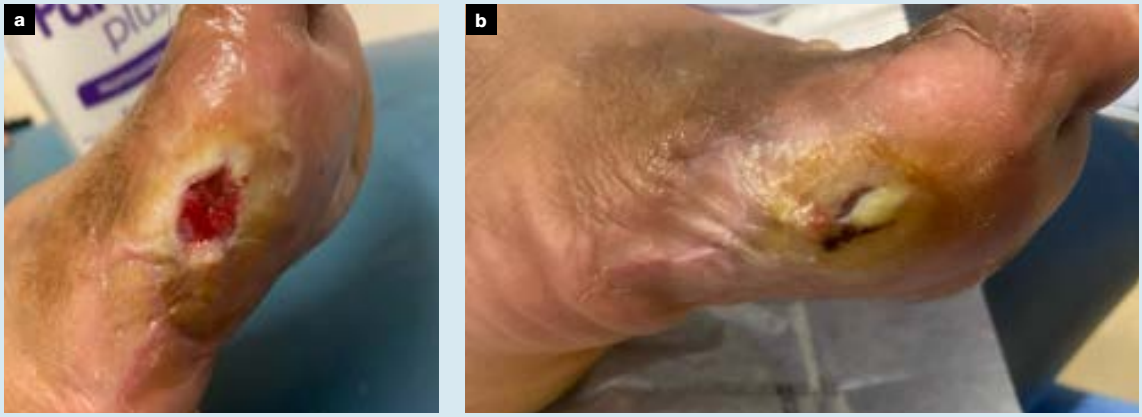
The integration of a chemical debridement agent, such as a TDA, and advanced xenograft technologies, such as an OFM containing hyaluronic acid, presents a promising approach for managing hard-to-heal wounds. The desiccating gel used in this case, with its rapid biofilm and devitalised tissue reduction capabilities, produces a conducive environment for healing. It does this by effectively disrupting microbial biofilms, and creating acidic conditions in the wound bed that can also denature proteins and disrupt bacterial membranes, making bacteria more vulnerable to immune clearance or topical antimicrobials.[11] The TDA used on this patient is a strong acid with a ≈pH of 1.0. This aligns with findings from Cogo et al.,[12] who demonstrated significant improvements in biofilm-laden hard-to-heal (chronic) wounds with desiccating agents, resulting in

Fig 1. Following basic cleaning of the hard-to-heal lower extremity diabetic ulcer (LEDU) and periwound area, the single-use vial of a topical dessicating agent should be applied over the wound bed and 1cm of the periwound skin. After being left in place for 60 seconds, the gel is diluted, neutralised and removed by rinsing with saline or sterile water. After application, there is no specific requirement for dressings or other interventions, and these can be used at the clinician's discretion

Fig 2. The wound base may have a caramelised desiccated appearance after removal of the topical dessicated agent (TDA). This TDA is indicated for non-surgical debridement and treatment of hard-to-heal wounds that are either infected, contain biofilm or necrotic tissue. Several contraindications apply, including for ischaemic wounds before effective revascularisation; neoplastic wounds; underlying abscesses or fasciitis that require incision/excision and drainage; underlying osteomyelitis; exposed cartilage and/or intolerance or allergies to any of the product ingredients

Fig 3. After surgical debridement **(a)**, an ovine forestomach matrix xenograft containing a layer of hyaluronic acid was added to the patient's treatment regimen **(b)**

Fig 4. After three months of treatment, the surface area of the left lower-extremity diabetic ulcer (LEDU) had decreased by 88% and was progressing steadily towards complete closure **(a)**. After four more weeks, the LEDU had fully closed with 100% re-epithelialisation, successfully preserving the limb in a patient who had been at significant risk of amputation **(b)**



accelerated granulation and wound healing progression.

Similarly, an OFM xenograft containing hyaluronic acid can encourage progression along the wound healing cascade, serving as a scaffold for cellular infiltration and angiogenesis.[13] This is supported by Bosque et al.,[14] who reported improved outcomes in hard-to-heal wound management using ovine extracellular matrix (ECM) grafts, highlighting their role in enhancing tissue regeneration and reducing healing time.

Khalaf[15] reported rapid healing in challenging calciphylaxis cases with the ovine ECM, highlighting its versatility across atypical and hard-to-heal wounds. Moreover, Brice et al.[16] demonstrated its efficacy in rural settings with complex patient profiles, achieving significant percent area reduction, even in resource-limited environments.

Economic analyses by Guest et al.[17] underscored the cost-effectiveness of integrating advanced therapies, such as a TDA, into standard wound care protocols. For example, hard-to-heal venous leg ulcers (VLUs) treated with a TDA exhibited faster healing rates and reduced overall healthcare costs, emphasising its potential as a scalable solution in healthcare systems.[17]

In this case study, the combined use of these modalities resulted in an 88% reduction in wound area within 96 days, achieving complete closure in 110 days. This also emphasised their effectiveness in disrupting chronic inflammation and enhancing healing. Future research should be expanded to larger clinical trials to confirm these outcomes and examine long-term effects in various patient populations.

Conclusion

In cases of hard-to-heal LEDUs, combining chemical debridement via a TDA with hyaluronic acid-containing OFM xenografts could significantly reduce wound size and support healing, even in patients with poorly controlled diabetes. This approach may serve as a valuable alternative to traditional care practices, enhancing patient outcomes and reducing the burden of LEDUs, such as DFUs. JWC

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Reflective questions

- How does the mode of action of the topical dessicating agent (TDA) used in this study differ from traditional debridement methods, and what advantages does it offer in promoting wound healing, particularly in hard-to-heal wounds, such as diabetic ulcers?
- How does the TDA used facilitate effective wound bed preparation, and what specific role does its chemical desiccation process play in optimising the wound environment for successful integration and performance of the ovine forestomach matrix (OFM) xenograft?
- What properties of OFM contribute to optimising moisture retention, reducing inflammation and supporting cell migration?