1. Abstract

A 64-year-old male presented with a diabetic foot ulcer measuring 1.3 cm2 in circumference. Patient's wound was treated using DermaBind TL (formerly AmnioBind), a terminally sterilized, dehydrated, full-thickness placental membrane allograft consisting of amnion, chorion, and the associated intermediate (spongy) layer. Treatment consisted of wound debridement, covering the wound with DermaBind TL, and covering the wound with gauze. Every 6-7 days the gauze was removed, the wound debrided, and new DermaBind TL allograft applied. Treatment proceeded for 3 weeks in which time the wound was reduced to 0.09 cm2 in circumference.

2. Introduction

As the largest organ of the human body, the skin has a significant impact on various human activities and functions, including protection from pathogens, sensing of the external environment, and thermoregulation [1]. However, as the outermost part of the human body, the skin, due to its elastic and soft nature, is prone to develop wounds [2, 3]. Although human skin is able to repair itself spontaneously to restore its structural and functional integrity, wound care is still paramount to prevent infection and dehydration, relieve pain, protect the open site, accelerate the healing process and prevent scarring, especially in large and open wounds or burns [4-6]. In 2014, there were 17.2 million hospital visits for acute wounds in the United States [7]. Currently, approximately 1-2% of the population in developed countries suffer from chronic wounds [8]. Meanwhile, chronic wounds such as diabetic ulcers, vascular ulcers and pressure ulcers, which have a long and cruel healing time due to disease, aging or inappropriate treatment, not only affect patients' daily lives, but are also associated with high morbidity and mortality [9, 10].

To date, the physiology of wound healing is well understood [11]. The healing process involves four overlapping phases: hemostasis, inflammation, proliferation, and remodeling [5, 12-14]. There are many types of wounds: acute incisional and excisional wounds can undergo a normal healing process, while chronic wounds have aberrant healing conditions [10]. In the clinic, wound healing management varies according to tissue characteristics, intrinsic regenerative capacity, wound classification, and other environmental variables [6, 10, 15-17]. Therapeutic strategies for wounds are diverse and include hyperbaric oxygen therapy [18-20], negative pressure therapy [21], vacuum-assisted closure [22], ultrasound [23], electrotherapy [24, 25], autografts/allografts and xenografts [4, 26, 27], cell-based therapy and engineered skin grafts [4, 28, 29], and topical drug and growth factor delivery [30-32]. Regardless of the wound class and the chosen wound management strategy, a wound dressing is required [33]. Traditional passive wound dressings such as gauze, bandage, and cotton wool would adhere to the skin tissue, causing dehydration and re-injury when removed. In contrast, allograft wound dressings integrate the multifunction of maintaining a moist environment, managing exudate and protection from pathogens, adhesiveness, and suitable mechanical properties have recently surged and demonstrated extraordinary advantages in more complicated situations [4, 34, 35].

3. Case

Patient in this case report is a 64-year-old male. Patient is a diabetic with an A1C of 6.9% and ABI of 1.1 upon presentation at the clinic. Patient currently uses Atorvastatin Calcium (10 mg), Docusate Sodium (100 mg), Lisinopriol (20 mg), Metformin (500 mg), Ondansetron (4 mg), Semaglutide (2 mg/3mL dose), and Tramadol HCl (50 mg). Patient does not abuse illicit drugs, alcohol, or tobacco. When this patient was presented at the clinic, he had an ulcer on the plantar surface of the right foot, Wagner Grade II. Ulcer failed conservative treatment for more than 6 months, the wound did not decrease by 50% in size within 4 weeks of wound development, despite conventional treatment of local wound care consisting of sharp debridement, treatment with Medihoney, Betadine Solution, and Aquacel Ag, and offloading in a Charcot Restraint Orthotic Walker (CROW).

Treatment of the diabetic foot ulcer immediately commenced. The existing bandage was removed, the wound area was then sharply debrided, rinsed lightly with saline, and a DermaBind TL allograft (2.0 cm x 2.0 cm) was placed directly on the wound. The allograft was then covered with cotton gauze. The allograft was left on the wound for 6 days at which time the wound was again debrided and a new allograft was placed on the wound. When a new allograft was applied (approximately each week), the circumference of the wound and depth of the wound were measured to assess progression of the wound toward closure. This treatment regimen continued for 4 weeks.

Based on previous uses of DermaBind TL, the expectation was that the wound would progress from the non-healing state to a healing state. A four-week timeline was not expected to result in a full closure of the wound but significant progress was expected to occur. Wound measurements are found in the following table:

Weeks	Wound Circumference (CM^2)	Infection Present?	% Reduction Circumference
0 (Inital Visit)	1.3	No	-
1	0.48	No	63.1
2	0.2	No	84.7
4	0.09	No	94.1

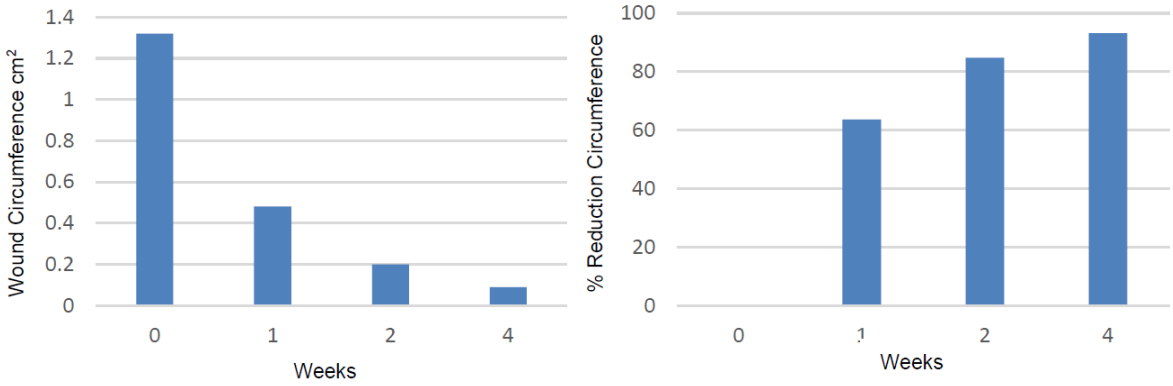

Figure 1. Graphical representation of: A) wound circumference, and B) Percent wound circumference reduction over a 4 week span

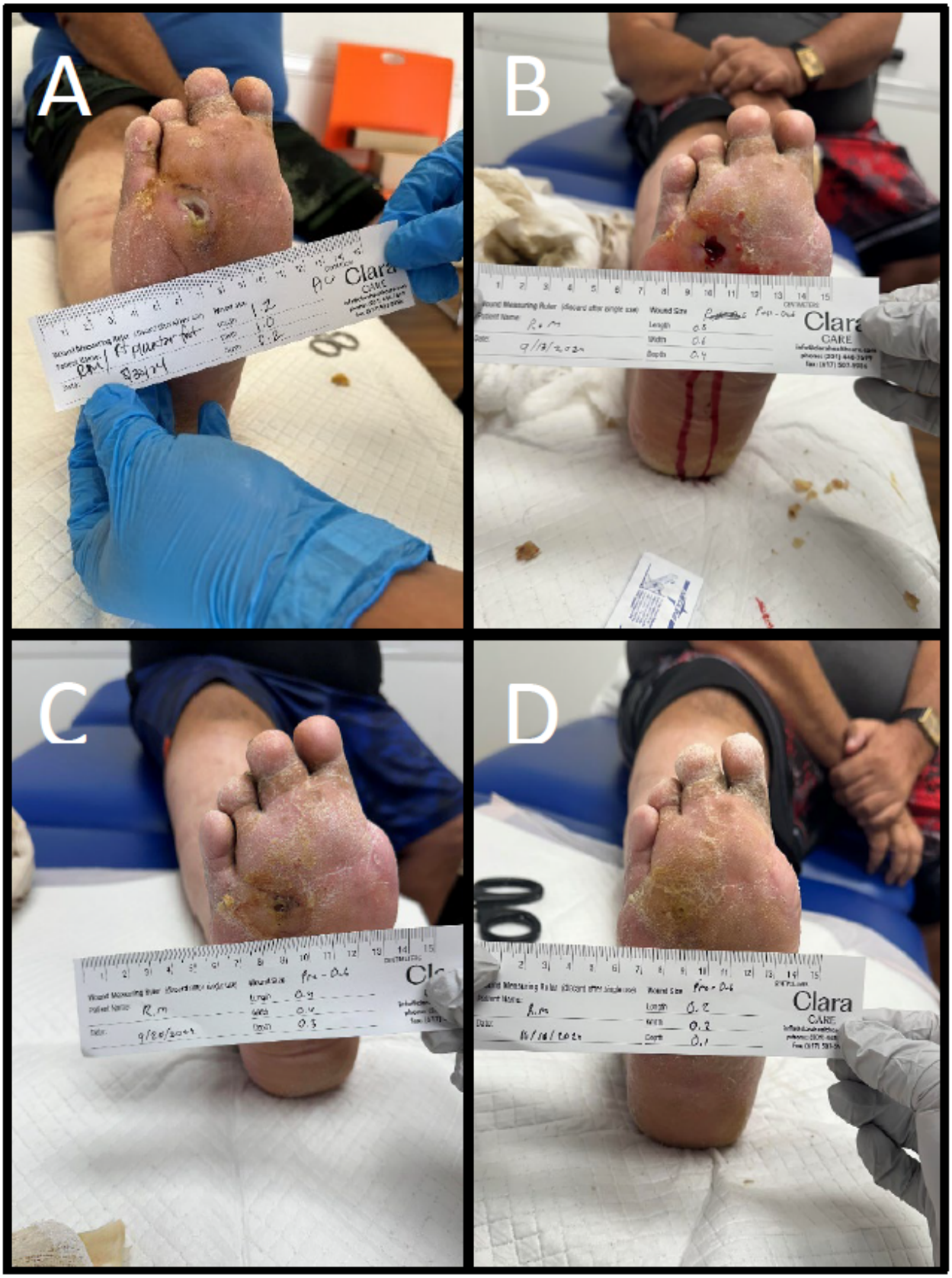

Figure 2. Wound photographs depicting: A) Initial visit, pre-debridement, B) Initial Visit, post-debridement, C) Week 2, and D) Week 4

4. Discussion

A patient, 64M, with a non-healing diabetic foot ulcer, was treated using DermaBind TL for 4 weeks. During this 4-week period, there was a significant reduction in the circumference and the depth of the diabetic foot ulcer. After 4 weeks of treatment, this wound had decreased in circumference by 94%.

The purpose of this case study was to assess the feasibility, ease of use and safety associated with the use of this novel full-thickness placental membrane allograft. The diabetic foot ulcer treated with DermaBind TL experienced at least a 50% reduction in wound area within 3 weeks of initial application. The authors believe that this is the only case reported in the literature of the use of this therapy. Considering that this patient had previously failed conventional wound treatments, the results obtained support the hypothesis that full-thickness placental membrane allografts are effective in promoting wound healing. No adverse events were observed in the study.

Human amniotic membrane has been used to promote granulation tissue in wounds for over a century. It has been shown to promote new vessel formation in leg ulcers and has bacteriostatic properties [36]. It is sometimes used in developing countries as a low- cost treatment for burns because it has been shown to reduce pain and speed healing [37]. It has been shown to increase the success rate of skin grafting in burn patients [38]. Amniotic membrane tissue is harvested from the placenta from mothers who are seronegative for HIV, sexually transmitted diseases (STDs), hepatitis C (HVC), and hepatitis B (HBS) tests, although it is often not feasible to use or store fresh amniotic membrane. Several amniotic membrane products are available to the clinician for use in wound management. These products may be dehydrated or cryopreserved and may contain amnion alone or amnion and chorion. The full-thickness placental membrane product used in this evaluation is composed of both amnion and chorion layers of amniotic membrane as well as the associated intermediate layer.

In the clinical setting, randomized controlled trials suggest that placental membrane derivatives can be used to effectively treat diabetic neurotrophic ulcers [39]. In the study by Zelen et al, patients were randomized to receive standard care alone or standard care with the addition of dehydrated Amnion Chorion Membrane (dHACM) every two weeks [39]. Significant differences in wound reduction were observed 4 weeks after the first application of dHACM, with a mean wound reduction of 32-0% ± 43-7% with standard care (n = 12) versus 97-1% ± 7-0% (P <0-001) with dHACM (n = 13). Overall healing rates after 4 and 6 weeks of treatment with dHACM were 77% and 92%, respectively, compared to 0% and 8-0%, respectively, with standard care (P <0-001). The treatment protocol used by Zelen et al. included biweekly application of a dHACM allograft, which is longer than the once-per-week application protocol in this study [39]. Although our observations were more limited in scope, the results obtained by other investigators suggest that research into multiple dHACM applications on wounds of different

sources is warranted and will likely yield further positive results in addition to those we observed. In fact, another randomized trial evaluated weekly versus bi-weekly application of dHACM for the treatment of diabetic foot ulcers and found that wounds treated with weekly dHACM application healed faster than those treated bi-weekly [40]. The mean time to healing was only 2-4 ± 1-8 weeks in the weekly dHACM group compared to 4-1 ± 2-9 weeks in the biweekly dHACM group (P = 0-039) [40]. Faster healing with weekly application provides an economic benefit in that these patients
require fewer visits and dressing changes to the wound care center and reduce their risk of adverse events.

Chronic wounds are burdensome in terms of both the negative impact on patient quality of life and the financial costs associated with their management. The development of effective, affordable and durable techniques for rapid wound closure is a priority for healthcare systems. Future research comparing the efficacy of skin substitute products and classes is clearly needed, as the current literature can only be used to evaluate product efficacy compared with standard wound dressing techniques. In addition to the efficacy of various skin substitutes, the cost of application must be considered. The investigation of shelf-stable, low-cost allografts could address current clinical concerns by making advanced allografts more widely available to both clinicians and patients by limiting expensive handling practices and production costs. Human amniotic membrane (dHAM) has unique biochemical properties that make it potentially applicable to wound care. dHACM has been developed as a potential vehicle for these properties in a shelf- stable form, limiting product cost and allowing for greater ease of use. The dHACM has been shown to be both clinically and cost effective compared to other advanced wound care products for the treatment of diabetic lower extremity ulcers [41-42]. Considering that DermaBind TL contains the amnion, chorion, and the intermediate (spongy) layer, it follows that a full-thickness placental membrane would have at least similar, if not better, results.

This non-randomized product study supports the hypothesis that placental membrane allografts can be used in chronic wound therapy. These data are consistent with data obtained in similar studies and build on the established history of placental membrane derivative use for non-healing wounds. Future research would require the performance of multicenter randomized controlled trials to evaluate the efficacy of placental membrane in the treatment of chronic wounds of various causes and whether full-thickness placental membrane is more effective in the treatment of these wounds than other currently available products.

5. Conclusion

DermaBind TL offers an effective and easy-to-use treatment alternative for the management of chronic wounds. Clinical improvement results strongly suggest significant and faster healing, resulting in complete wound closure, in wounds treated with full-thickness placental membrane-containing products. Chronic wounds that do not respond to other standard treatment options show significant healing and wound coverage with placental membranes. Easy storage and extended shelf life promote clinical acceptance in the wound care

environment. Lower complication rates compared to other similar products have been reported in numerous clinical studies. Although DermaBind TL has a higher unit (dressing) cost compared to standard wound care, the overall cost is similar or lower considering the faster healing and presumably lower rate of complications and clinical sequelae such as amputations.

6. References

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