

CASE SERIES DEMONSTRATING THE IMPACT OF DEHYDRATED HUMAN AMNIOTIC MEMBRANE ALLOGRAFT* ON WOUND HEALING IN ACUTE AND CHRONIC WOUNDS

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INTRODUCTION

Lower extremity ulcers in patients with diabetes and/or vascular disease are notoriously hard to heal and require chronic treatment with multiple and advanced modalities.¹ Because of prolonged healing time of diabetic foot ulcers (DFUs), there is an increased risk of morbidity, infection, hospitalization and amputation, therefore the primary goal of DFU treatment is rapid wound closure.^{2,3,4} Standard treatment includes management of underlying disease, wound debridement, infection control, off-loading and hyperbaric oxygen therapy.⁵

Unfortunately, despite the use of recommended wound management strategies, many DFUs do not heal. Some of the largest published studies reviewing the control groups of DFU studies have demonstrated healing rates of only 24.2% at 12 weeks and 30.9% at 20 weeks.⁶ Furthermore, a 50% reduction in wound size at 4 weeks has been identified as a critical cut-off point for evaluating diabetic foot ulcer treatment success.⁷ These data suggest the need for advanced therapies such as human skin equivalents, wound modulators and growth factors to be considered if wound area is not reduced by 50% after 4 weeks of conservative management.

DAMA* is a dehydrated human amniotic-derived tissue allograft that provides an intact extracellular matrix that provides structural tissue to advance soft tissue repair, replacement and reconstruction. Amniotic tissue contains growth factors and biological macromolecules and has been used to treat a variety of wounds due to its non-immunogenic⁸, anti-inflammatory⁹ and anti-bacterial¹⁰ properties.

Clinically, the positive impact of cellular tissue based products on DFUs has been reported in several RCTs, case series and retrospective studies. In general, an improvement in wound size has been observed within 2-3 weeks with a percent area reduction (PAR) of 40-50% within 3-4 weeks.² However, there is a wide range of success with a percent area reduction (PAR) up to 98.4% reported in one clinical trial.¹¹ Similarly, the percent of wounds achieving closure at 12 weeks have ranged from 30%-76%.¹¹ The reason behind the range of data may include the different study designs, graft product characteristics, baseline wound size and duration and frequency of graft application.

The current case series aims to illustrate the use of DAMA in a variety of wounds. It includes 2 acute wounds and 4 chronic wounds in patients with diabetes and/or vascular disease, including a challenging case of necrobiosis lipoidica diabetorum.

METHODS

All patients were treated at the Wayne Memorial Wound Care Center. For the acute wounds, DAMA was applied after 1-2 weeks. In the chronic wounds, DAMA was applied after a failure to demonstrate a 50% reduction in wound size after 4 weeks of treatment with advanced wound care, off-loading and other standards of care. As such, for the chronic wounds, DAMA was applied after a mean of 12 weeks (range 9-35 weeks).

Before application of DAMA, surgical wound bed preparation was completed to ensure the wound was free of clinical signs of infection or decaying tissue.

Every 1-2 weeks, wounds were assessed, measured, photographed and wound appearance and wound care strategies employed were documented.

RESULTS

Six patients were included representing 2 acute wounds and 4 chronic wounds. The acute wounds were present for an average of 1.5 weeks (1-2 weeks) and the chronic wounds were present for an average of 17.8 weeks (9-35 weeks), before application of DAMA.

For the chronic wounds, the mean baseline wound area was 1.93 cm². In these wounds, in addition to standard wound care practices; each patient had tried one or more advanced wound care therapies without success prior to using DAMA (see Table below).

CHRONIC CASES	PREVIOUS TREATMENTS THAT FAILED TO CLOSE WOUND(S)
Case 1	Silver nanocrystalline dressing ¹² , Bi-layered bioengineered skin substitute ¹³ , Hydrofiber dressing ¹⁴
Case 2	Bi-layered bioengineered skin substitute ¹³ , Hydrofiber dressing ¹⁴
Case 3	Protease modulating collagen dressing ¹⁵ , Protease modulating collagen dressing with silver ¹⁶
Case 4	NPWT, HBO

In both acute and chronic cases, all wounds showed marked improvement, including a decrease in wound size, within 2 weeks following the first application of DAMA. By 4 weeks, the application of DAMA led to a mean wound volume and area decrease of 82.5% and 60.5%, respectively. At 6 weeks following the first application, a mean decrease of 91.3% and 86.28% was demonstrated for wound volume and area respectively (Figure 1).

For the chronic wounds, DAMA was used in complex patients for challenging wounds that experienced slow or stalled healing after standard wound care and at least 1 trial of other advanced wound care therapies such as other cellular tissue based products. In these patients the average PAR in the 6 weeks prior to DAMA application was only 1.8%. In the 6 weeks after DAMA was initiated a mean PAR of 86.3% was observed, demonstrating the successful initiation ("kick start") of wound healing in these previously stagnant wounds (Figure 2).

In the acute wounds, the wounds closed in an average of 1.5 weeks (1-2 applications) and in the chronic wounds after a mean of 7.5 weeks (3-4 applications). All wounds were closed by 8 weeks. (Figure 3)

CONCLUSIONS

- In the current case series, DAMA has a positive impact on wound healing in a variety of acute and chronic wounds.
- In the chronic wounds, the positive impact on DAMA was demonstrated in challenging wounds that experienced an absence of, or slowed, healing with advanced modalities such as NPWT and bi-layered bioengineered skin substitutes.
- In these cases, a mean 60.5% PAR was achieved at 4 weeks which is well above the recommended 50% PAR in 4 weeks indicating treatment success.
- PAR of 86.3% at 6 weeks and 100% of wounds achieving closure by 8 weeks is positive in comparison to the range of clinical results seen with bioengineered substitutes.
- All the chronic wounds closed by 8 weeks in these very difficult-to-heal wounds, with the presence of venous and arterial disease and/or poorly controlled diabetes, which makes the rapid progression to closure even more remarkable.
- Overall, the results illustrate the role for DAMA in the support of healing for both acute and chronic wounds; particularly wounds that have stalled or slowed healing or where risk factors exist that make quick closure a priority.

Figure 1

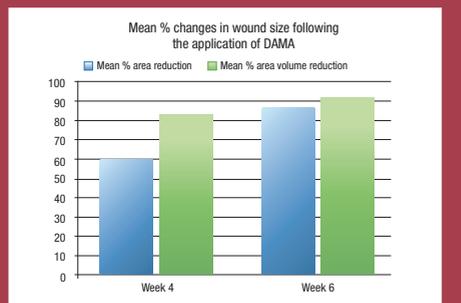


Figure 2

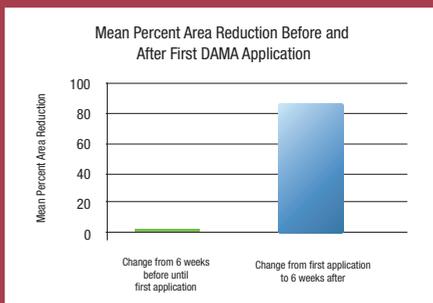
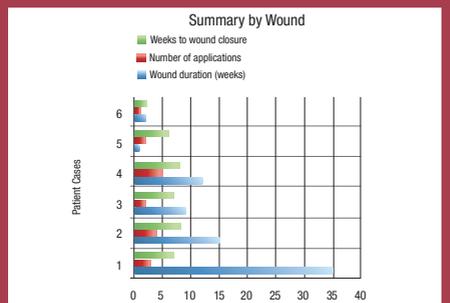


Figure 3



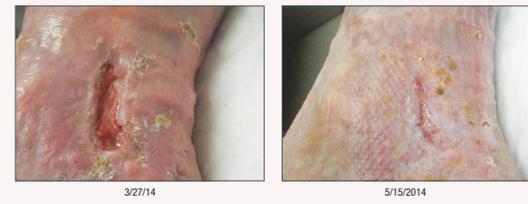
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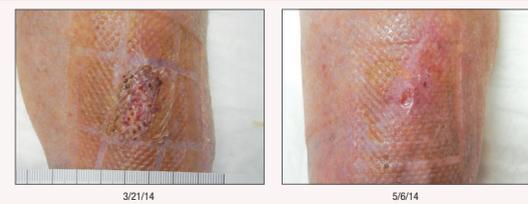
CASE 1

A 64-year-old male with a history of long-standing venous disease and 5-6 years of ulcerations. He is a smoker who has diabetes (HbA1C=8.4%), hypertension, chronic venous insufficiency and peripheral arterial disease (PAD). He presented with a venous leg ulcer on his right medial malleolus. The initial wound measured 3.8 x 1.5 x 0.2 cm. It was a large full thickness ulceration with significant slough and bioburden. Following surgical debridement, the wound bed remained very fibrotic. The wound had slight peri-wound erythema and tenderness to palpation. Previous wound treatments included: high grade multilayer compression wraps, a bi-layered bioengineered skin substitute¹³, which was used 5 times without a significant impact on wound healing. After a lack of marked progression after 2 months of advanced treatments, DAMA was applied at week 35. Within 2 weeks, marked improvement was noted in wound size. DAMA was applied every 2 weeks with a total of 3 applications until the wound closed at 6 weeks.



CASE 2

A 74-year-old male with history of chronic venous insufficiency with DVT presented with a traumatic wound to his lower left anterior leg after striking his leg with a leaf blower. His medical history included sarcoidosis, peripheral vascular disease, recurrent phlebitis, DVT and foot drop on the left side. The initial wound measured 5.9 x 5.2 x 0.2 cm. The wound was treated with a variety of advanced wound care strategies including 2 applications of bi-layered bioengineered skin substitute¹³ without significant success. Therefore, at 15 weeks duration, DAMA was applied. Within 2 weeks, a significant decrease in wound size was observed. DAMA was applied every 2 weeks (4 applications total) until the wound closed at 8 weeks.



CASE 3

A 47-year-old obese female with a history of diabetes (HbA1C=8.4%), venous insufficiency and necrobiosis lipoidica diabetorum (NLD) presents with an open ulceration that developed spontaneously on her lower left anterior leg, an area where she had pre-existing NLD. NLD is a rare complication with a reported frequency of 0.3% in diabetic patients.¹⁷ It occurs when collagen degenerates, deposits of fat build up and the blood vessel walls thicken causing wound healing to be extremely impaired.¹⁴ She had significant edema. The initial wound measured 1.0 x 1.8 x 0.2 cm. Her leg improved following initiation of compression as her edema becomes well controlled. In addition to standard wound care management, treatment with protease modulating collagen dressing¹⁵ and protease modulating collagen dressing with silver¹⁶ was initiated. However, after some improvement, the healing again stalled and the wound began to increase in size. DAMA was then applied at which point, the wound had been present for 9 weeks. A significant impact on wound size and appearance was noted within 2 weeks. DAMA was applied again 2 weeks later until the wound closed at 6 weeks. This case was remarkable given the extremely challenging co-morbidities of venous insufficiency and NLD.



CASE 4

A 78-year-old male with diabetes (HbA1C=6.3%), CAD, hyperlipidemia & HTN presented with post-amputation wound at his great left toe site. Wound started as a small callous lesion. The lesion opened and became painful, red and swollen from his toe to foot leading to first toe amputation. 1 month later, he presented at the clinic with a neuro-ischemic wound at the amputation site. Due to his severe PAD, he was sent for a vascular surgery consult, finding an ABI of 0.79 and the assessment concluded that the diminished digit brachial indices and digit pressure were not conducive to wound healing. He underwent endovascular reconstruction followed by surgical revision of first toe amputation 1 month later. He was then referred to the clinic with wound measuring 4.0 x 3.3 x 0.6 cm. The wound had significant circumferential erythema at least 2 cm beyond the wound margin and distal third of his lower leg was edematous, tight and shiny. The wound bed had very minimal healthy granulation tissue with mostly necrotic tissue. After 1 month of limited progress with standard wound care strategies, he was treated with NPWT. Approximately 7 weeks post-revascularization, his toe pressures had diminished to 25 mmHg, which is consistent with poor to no wound healing. Due to the slow rate of wound progression, DAMA was initiated at week 13. Within 2 weeks, the wound was more granular (95%) and decreased in size. DAMA was applied every 2 weeks, 4 applications total, until the wound closed at 8 weeks.

