The use of Human Fibroblast Derived Dermis on Post-Surgical Wound Dehiscence: A report of two cases

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Abstract:

Human fibroblast derived dermis (Dermagraft®, Advanced BioHealing, La Jolla, CA) is currently being used in the treatment of diabetic foot ulcers as an adjuvant therapy. Dermal skin equivalents have gained acceptance by many different disciplines for complicated or hard to heal wounds based on their efficacy. Dermagraft is a sterile, dermal substitute, derived from human fibroblasts, which contains key active components shown to compliment wound healing. Dermagraft contains essential growth factors, matrix proteins, and glycosaminoglycans (GAGs) that participate in wound closure. This product is derived from neonatal foreskin fibroblasts that are populated onto a bioabsorbable scaffold. Currently, Dermagraft® is indicated for the treatment of full thickness diabetic foot ulcers greater than 6 weeks duration without exposed tendon, joint capsule or bone. The purpose of this review is to report on a novel off-label use of this product in the treatment of high-risk diabetic patients with post-surgical wound dehiscence.

Introduction

Diabetic foot ulcers are a major cause of lower extremity amputations.¹⁴ In diabetic patients, seventy to eighty-five percent of lower-limb amputations are preceded by a chronic foot ulcer.²,⁵ More than fifteen percent of all diabetic patients will develop a lower extremity ulcer at some point in their lifetime.³,⁴ It has been well established that the biological behavior of chronic wounds differs from that of acute wounds.⁶ However, when comparing diabetic wounds vs. non-diabetic wounds, these comparisons are less clear.⁶ Many factors have been identified in order to understand the impaired healing of wounds in diabetic patients, which includes, but is not limited to, vascular disease, tissue hypoxia, aberrant cellular and inflammatory pathways, as well as, peripheral neuropathy.²,⁶ When looking at aberrant cellular components, irregularities in fibroblast and neutrophil function have been found among individuals with diabetes.⁷,⁸ Moreover, it has been shown in vivo that hyperglycemia may be harmful to these cellular components.⁸ These cellular differences have not been specifically demonstrated in vivo, yet the production of end product glycosylation found in diabetes has been shown to affect cell function and lead to delayed healing and chronic wounds.⁸

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Included in the spectrum of diabetic wound complications are post-surgical complications, with a rate ranging from 27% to 87.1% in patients undergoing transmetatarsal amputation.\textsuperscript{9-13} Postsurgical complications include, stump infarction, wound dehiscence, skin breakdown, additional surgical procedure including debridement, and the necessity for a more proximal amputation to name a few.\textsuperscript{9-13} Post-surgical wounds and chronic foot ulcers in diabetic patients have been shown to exhibit a more dysfunctional biology than what has been observed in the acute wound-healing cascade.\textsuperscript{7,8} These identified components related to chronic wounds and delayed healing in diabetic patients afford targets for advanced therapies and novel approaches.

Advanced cell-based wound therapies have been on the market for over a decade and have gained acceptance by many different disciplines for complicated or hard to heal wounds based on their efficacy. Dermagraft® (Advanced BioHealing, La Jolla, CA) is a sterile dermal substitute derived from human fibroblasts and contains key active components shown to compliment wound healing. It contains essential growth factors, matrix proteins, and glycosaminoglycans (GAGs) that participate in wound closure.\textsuperscript{14} This product is derived from neonatal foreskin with fibroblasts populated onto a bioabsorbable scaffold.\textsuperscript{15}

Dermagraft® provides a human dermal scaffold for fibroblasts that deposit matrix proteins.\textsuperscript{16} The wound healing process is coordinated by the activity of the fibroblasts in the dermal layer. Keratinocytes surrounding the ulcers are then able to adhere, proliferate, differentiate and migrate across the single layered dermal matrix.\textsuperscript{14,16} Hanft et al. reported a 71.4% wound closure by week 12 compared to 14.3% in the control group.\textsuperscript{14} Currently, Dermagraft® is indicated for the treatment of full thickness diabetic foot ulcers greater than 6 weeks in duration that do not exhibit exposed tendon, joint capsule or bone.\textsuperscript{14}

The purpose of this study is to report on the use of this fibroblast derived dermis in a VA setting with a large diabetic and “high risk” patient population in an off-label use. Therefore, we present two cases where human fibroblast derived dermis was used in post-surgical wound dehiscence in patients with diabetes for limb salvage.

**Case Presentations**

**Case #1**

A 61 year old male with a history of diabetes, peripheral neuropathy, deep vein thrombosis, and prior left transmetatarsal amputation presented with a right foot sub first metatarsal head ulceration. The ulceration did not probe to bone and there were no clinical signs of infection. He underwent surgery for a right foot pan metatarsal head resection. Nineteen days post-operatively signs of complete wound slough and dehiscence overlying the 1st metatarsophalangeal joint was appreciated. (Fig 1) The wound was approximately 3 cm in length, 1 cm width and 0.5 cm deep to extensor hallucis longus (EHL) tendon. The wound site had no signs of infection and was treated with daily wet to moist dressing changes with normal saline gauze packing. After 9 days, the treatment was changed to Dermagraft® due to inadequate wound progression. The dermal replacement was placed overlying the tendon at a frequency of once weekly. Standard debridement was carried out weekly prior to each application of the tissue implant. Five applications were utilized in order to achieve complete epithelization of the wound and a satisfactory surgical outcome. (Fig 2)

**Case #2**

A 55 year old obese male with a history of diabetes, diabetic neuropathy, hypertension, hyperlipidemia, left transmetatarsal amputation (TMA) and right hallux amputation presented with a non-healing ulceration sub 2nd metatarsal head with radiographic and clinical evidence of osteomyelitis.
Surgical management included a right transmetatarsal amputation with primary closure. Four weeks post-operatively the patient presented to the treating surgeon’s office with two areas of surgical site dehiscence medially and centrally. (Fig 3) Total wound length and width was approximately 2 cm. The maximum depth of the dehiscence area was approximately 1 cm. The wound site had no signs of infection and was treated with Dermagraft®. Weekly serial debridement along with the application of the tissue product and a total contact cast was utilized. Five applications of the dermal replacement were used in order to achieve a satisfactory surgical outcome with complete wound closure. (Fig 4)

Conclusion

Diabetic foot ulcers are frequent complications associated with diabetic neuropathy and are known to be associated with increased morbidity and mortality as well as higher health care costs. Complications associated with limb salvage secondary to diabetic foot ulcers have also been shown to have a high rate of morbidity. Living tissue equivalents have been shown to increase the healing rate for diabetic foot ulcers over standard wound care regimens. In these case examples, a dermal replacement product was successfully utilized in an off-label use on post-surgical wound dehiscences without complication. Further study is warranted in this area.
Figure 3  Case 2. Four weeks post-TMA two areas of surgical site dehiscence are seen medially and centrally.

References


Figure 4  Case 2: Healed incisions after five applications of the dermal replacement therapy.