Utility of Fish Xenograft in Plantar Foot Ulcerations

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Statement of Purpose

This study aimed to assess the utilization and efficacy of omega-3 fatty acid fish xenograft in the setting of diabetic plantar foot ulcerations. Fish xenograft has shown favorable results in the application of lower extremity wound care with several key benefits. Such include its similar microscopic structural makeup which nearly mimics that of native human skin. Additionally, it is comprised of a durable and thickened matrix in which it provides a scaffold for proliferative cell binding making it ideal for utilization in weight bearing surfaces of the foot.

Level of Study

Level IV Case Study

Introduction

Diabetes is a systemic disease that plagues multiple organ systems simultaneously. The diabetic foot and associated ulcers in particular are one of the most frequent complications occurring in nearly 4-10% of the diabetic population and often found coupled with PAD and/or neuropathy[1]. Even further, in the presence of ulceration, there has been a recorded 5-24% likelihood of future amputation.[1]

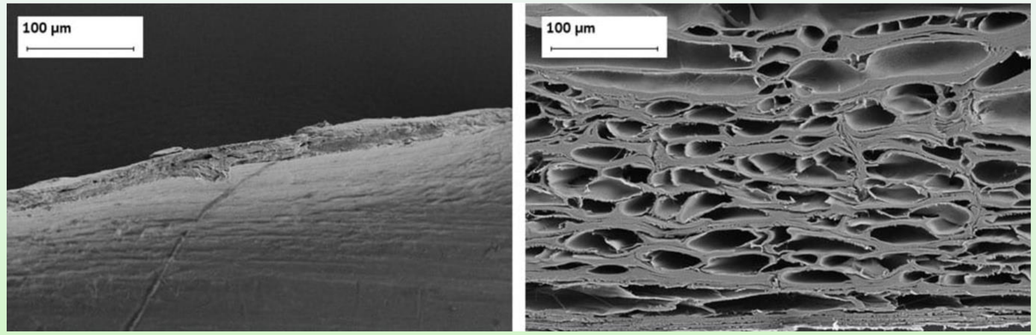
Diabetic foot wounds and infections vary in severity and presentation, some remaining within the depth of soft tissue planes and others penetrating to the level of bone. Bony involvement occurs in upwards of 20-66% of cases[1]. The PTB test, often utilized as a positive predictor for osteomyelitis, has been historically studied demonstrating a sensitivity of 66%, specificity of 85%, PPV of 89% and a NPV of 56%[2]. Infections with bone penetration often lead to more complex treatment regimens including repetitive surgical resection and prolonged antibiotic therapy. When deeper levels of infection and bone involvement are coupled with high risk locations including the plantar foot, the recipe often worsens. Uncomplicated plantar foot ulcers heal in 6-8 weeks if appropriate offloading techniques are implemented e.g. TCC. While these are not always readily available nor are patients often amenable to such treatment, another important factor is thus achieving adequate soft tissue coverage meaning full epithelialization of the wound bed. This may be achieved in many ways, most frequently to include allograft biologics and NPWT if primary closure is unable to be performed.

A systematic review performed in 2019 demonstrated wounds treated with biologics were 1.67x more likely to heal in 12 weeks versus standard of care dressings[3] . Within the last several years, acellular dermal matrices (ADMs) have become increasingly more popular. ADMs with Omega-3 in particular have shown promising applications in wound care of the lower extremity as it aims to decrease the inflammatory response while promoting proinflammatory cytokines and thereby healing. In addition, its structural makeup on a microscopic level nearly mimics that of native skin. Its significantly thicker matrix in which to provide a scaffold for proliferative cells to bind to makes it ideal for weight bearing surfaces of the foot given increased durability.

All factors combined, the acellular xenograft may prove to have great utility in the realm of diabetic plantar foot ulcers.

Methods

46 subjects with T2DM underwent application of omega-3 fatty acid fish xenograft secondary to plantar foot ulcerations between October 2020 and April 2023. Demographics included an average age of 63 between 35 males and 11 females. Comorbidities included but were not limited to CHF, HTN, charcot neuroarthropathy and obesity. Treatment algorithms were implored consisting of multiple debridement with bone resection as indicated with several requiring the addition of NPWT. Grafting was performed either intra-operatively or in the outpatient clinic setting. Serial grafting was required for larger, complex wounds with significant soft tissue defect. Some requiring repeat applications which occurred every 3-4 weeks. Extended duration IV antibiotics were determined by infectious disease colleagues based off proximal bone margins. Post operative course consisted of adhering to strict non weight bearing instructions in either a post op shoe or CAM boot.



Scanning electron micrograph of a fish xenograft (right) cross section with a complex 3D structure compared to that of other allograft wound products (left)

Results

All subject and clinical outcomes were evaluated demonstrating a 100% rate of healing as defined by full epithelialization of deep or exposed soft tissue and bone utilizing fish skin xenograft. The average wound size measured 9 cm^2 (range 2-19 cm^2) with an average patient A1c of 9.6% (range 7.9% – 12%). Approximately 32% of patients experienced full wound healing within 2-3 weeks with a single application of fish xenograft with a recurrence rate as low as 5%. Of note, 38% were not compliant with weight bearing restrictions however still proceeded to experience full wound healing.

Photos above demonstrating plantar wound healing over course of 3 months with 2 graft applications

Discussion

The diabetic foot in the setting of ulceration can lead to devastating outcomes especially in the face of peripheral neuropathy and peripheral arterial disease. With 5-24% of nonhealing ulcerations leading to primary amputation within 6-18 months it remains of utmost importance that these wounds are addressed both quickly and efficiently to prevent unwanted limb loss[1]. Appropriate debridement, utilization of offloading techniques, and appropriate wound dressings play significant roles in wound healing. Additional utilization of adjunctive biologics has shown great promise in expediting healing as well as in providing structural support and integrity to wound beds especially in the setting of high-pressure regions such as the plantar foot.

Fish skin xenografts may play a significant and beneficial role in promoting full epithelization in the setting of diabetic foot ulcerations and infection and subsequently healing of plantar foot defects as proven in this study demonstrating a 100% patient success rate.

Uncomplicated plantar foot ulcers generally heal within 6-8 weeks if appropriate offloading techniques are implemented e.g. utilizing total contact casting and other such tools. At times, these options are not readily available in clinic nor are patients amenable to such treatment.

Utilizing fish xenograft as an alternative can expedite wound healing to as low as 2-3 weeks with just a single application as highlighted by this study which is significant especially in respect to the plantar tissues. Warriner et. al performed a study demonstrating a 50% reduction in wound size at 4 weeks is a crucial cut-off point in predicting healing success.[5] Therefore, obtaining quick and efficient wound coverage and expediting healing progress is a time sensitive matter.

Waajiman et. al noted ulcer recurrence is as high as 42% within a span of 18 months.[4] With only 2 of 46 patients (5%) experiencing re-ulceration this low rate of recurrence places emphasis on the thickness, strength and durability that this newly developed matrix provides to the plantar tissues. Even when faced with patient non-compliance, fish xenograft has still demonstrated great success as highlighted by the 38% of non-compliant patents who still went on to full healing.

Further research with randomized control trials is necessary to further demonstrate and study the long term effects of fish xenograft in the setting of plantar foot ulcerations. However, this case series does shed light on how impactful fish xenograft can be within the diabetic cohort.

References

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