# Bio-Preserved Cellular and Stem Cell Therapies for Stage IV Pressure Ulcer

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## Introduction

The patient is a 33 year-old male who sustained a C6 American Spinal Injury Impairment Scale (AIS) Class A traumatic spinal cord injury (SCI) and right brachial plexopathy secondary to a vehicle rollover crash. He sustained multi-level cervical spinal fractures, requiring C6-T1 laminectomies, C5-T1 fusions, C5-6 and T1-2 vertex hardware fixation. His comorbid injuries during acute hospital course included right pneumothorax, multiple wounds and fractures of extremities and face, and urinary tract infection (UTI). He underwent dobhoff placement via EGD, bronchoscopy, chest tube removal, and tracheostomy on ventilator.

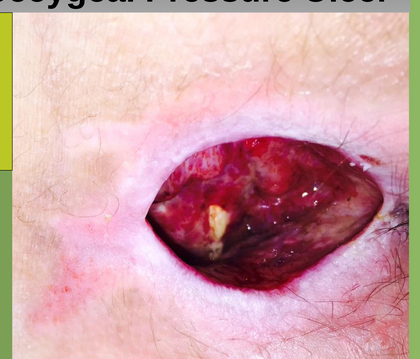
He was admitted to SCI center 45 days post-injury. He was noted to have a stage III pressure ulcer at the coccyx measuring 5cm X 2.6cm, yellowish slough present, with surrounding blanchable skin. Wound care team was consulted.

## Rehabilitation Hospital Course, Workup, Medical Treatment

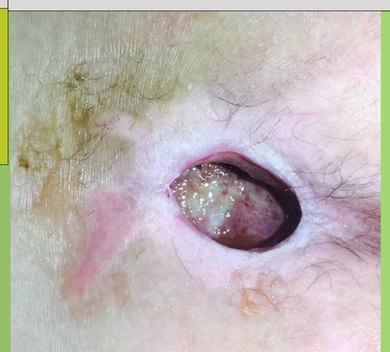
| Date (Post-Injury) | Pressure Ulcer Management | Pressure Ulcer Measurements and Dimension & Remarks |
|---|---|---|
| Initial (SCI Rehab Admission 45-53 | • Cleaning with normal saline daily and application of Santyl® to the area of slough. The wound was dressed with Xeroform® and covered by Mepilex®.<br>• Low air loss SPORT therapy bed, turning and repositionig with assistance q2h and prn | • 5cm X 2.6cm, yellowish slough present, with surrounding blanchable skin |
| 53-75 | • Add MIST therapy 3x/week<br>• ROHO cushion was mapped and fitted for his wheelchair<br>• Sharp debridement | • 7 x 2.5 x 0.3cm, 90% pink and clean, 10% devitalized tissue |
| 87 | • Antibiotic including Vancomycin and Piperacillin/Tasobactam were started for suspected wound infection with osteomyelitis | • Fever, leukocytosis, tachycardia<br>• 6 x 4 x 3cm with large amount of sanguinous drainage and deep tissue injury (DTI) to the distal wound base<br>• Stage IV sacro-coccygeal pressure ulcer<br>• CT scan of sacrum showed stage IV pressure ulceration extending down to bone with exposed bony spicules |
| 94 | • Surgical bone biopsy and debridement<br>• Antibiotic regimen was changed to Vancomycin & levofloxacin for a 6 weeks course<br>• Negative pressure device was placed on the sacral pressure ulcer | • Bone biopsy culture confirmed E cloacae, E faecalis osteomyelitis.<br>• 4.8 x 3 x 4cm with undermining and serous drainage |
| 111-118 | • **OASIS®** was applied, and re-applied 1 week later | |
| 122-142 | • Dressing was changed to Promogran and Aquacel Ag covered by Mepilex<br>• Bed rest , later discontinued for not improving with such measure | • 4.5 x 3 x 2.9 cm with tunneling and less purulent discharge |
| 170 | • Clinitron bed and limit out of bed only to therapies | • The wound regressed with increased bone exposure and undermining<br>• Possible colostomy with wound vac placement vs skin graft was discussed. |
| 188 | • **Grafix®** core 2 x 3cm was applied to wound bed over exposed bone;<br>• 1cc **Grafix®** prime injected into periwound tissue using sterile #22g needle and aseptic technique | • 2.8 x 2.5 x 3 cm |
| 209 | • **Epifix®** was applied | • 2.8 x 2 x 3 cm with undermining and palpable bone |
| 226-242 | • Negative pressure device was discontinued<br>The wound bed was lined with Promogran, lightly pack with Aquacel Ag | • 2.5 x 1 x 2.4cm with less undermining and mild serous discharge.<br>• 2 x 1 x 1.5 cm, dimensions of undermining continued to decrease at the end |

## Progression of Sacro-Coccygeal Pressure Ulcer

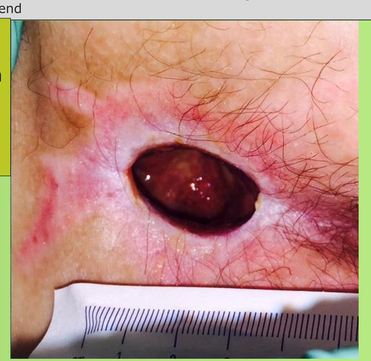
Day 90: Prior to application of bio-preserved cellular therapies



Day 170: At the beginning of bio-preserved cellular therapies



Day 226: Upon completion of bio-preserved cellular therapies



## Discussion

With the advancement of preservation techniques, there is a surge of new bio-preserved cellular and stem cells therapy. However, no large-scale randomized controlled study was applied to pressure ulcers in SCI population. This case demonstrates the trial of a combination of multiple products to salvage a non-healing pressure ulcer that was on the verge of surgical treatment.

Grafix®: a human viable wound matrix (hVWM), designed to preserve the native components of the human placental membrane in a cryopreserved product. Grafix® is produced using aseptic cryopreservation which claims to prevent cell loss from dehydration and radiation[1,2]. In a randomized single-blind study for diabetic foot ulcers, Grafix® was reported to reduce wound healing time comparing to control and to have a lower incidence of wound-related infections[3]. It was reported that Grafix® has 7.5 times increase in the angiogenic growth factor vascular endothelial growth factor (VEGF) as compared to dehydrated amniotic membrane[4].

Epifix® is dehydrated human amnion/chorion membrane (dHACM) therapy. It processes a chorionic layer, which contains additional beneficial molecules including collagen, connective tissue, cytokines and growth factors, which facilitate wound healing[5,6]. In a prospective, randomized, controlled study, Epifix® achieved complete wound closure and reduction in wound area in diabetic wound ulcer when compared to 2 control groups using standard of care and Apligraf®, a living, allogeneic bi-layered cultured skin substitute derived from human neonatal male foreskin tissue(7). Overall, Bio-preserved cellular and stem cell therapies aim at facilitating wound healing by their properties of anti-inflammatory, antioxidant, cell recruitment, and angiogenesis.

In this case, the patient's pressure ulcer site achieved significant reduction in size, clearance from osteomyelitis without recurrence s/p a course of antibiotics. Application of bio-preserved stem cell therapies were applied successfully in combination with negative pressure device and low frequency ultrasound therapy without side-effects. Regardless of the advance of wound care preparation, off-loading by pressure relief remains the single most important factor in wound healing.

## Conclusion

It is a combination of pressure relief and wound care that facilitated healing of his pressure ulcer. No single product clearly achieved the reduction in size. Future randomized control trials of various bio-preserved cell therapies for pressure ulcers in spinal cord injury population are necessary to demonstrate their potential efficacy.

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