Application of Umbilical Cord Tissue Allografts in Sacral Decubitus Ulcers: A Case Study and Review of Literature

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Abstract

Each year, thousands of patients suffer from sacral decubitus ulcers, also known as pressure ulcers or sores. Late-stage pressure sores present a unique challenge to physicians, in particular when they are deep, tunneling, and have tendon or bone involvement, as is the case for the two patients in this case study. At the time of consultation, both patients had wounds that were classified as Stage IV with tissue loss and involvement of bone or tendon. This case study demonstrates a precedent for applying Wharton's Jelly allografts in late-stage sacral decubitus ulcers with associated tunneling in combination with standard care.

Introduction

- 2.5 million new pressure ulcer cases each year with approximately 60,000 patient deaths annually (4,5,6).
- Pressure Sores are categorized into four stages with the fourth stage being the most serious (3).
- Stage IV pressure ulcers are deep wounds that can affect the muscles, bones, and ligaments. They are characterized by black skin, a hallmark of tissue necrosis, and are typically are contaminated by body fluids or infection (3).
- It may take as little as 1-2 hours to develop a stage III or IV pressure sore with 83% of bedridden patients developing decubitus ulcers within the first five days of hospitalization (1,2).
- Wharton's Jelly contains fibrous collagen types I, III, V, hyaluronic acid, and other glycosaminoglycans that catalyze healing (7).

Patient History

Patient 1

- Sustained a gunshot wound in 1975, resulting in paralysis
- Developed a pressure ulcer that became infected in 2016, resulting in the removal of the coccyx and surrounding fascial tissues (wound measurement 16cm x 8cm)
- At the time of referral to this study, the patient presented with a mid-sacral pressure sore with exposed tendon, bone, and tunneling lasting over ten years
- Patient was inconsistent with at home care and appointment schedule during treatment

Patient 2

- Suffered a fall in March 2020, resulting in paralysis
- During post care facility stay, the patient had a significant abscess that developed into a large ulcer
- At the time of referral to this study, the patient suffered from an ischial pressure sore with exposed tendon, bone, and tunneling for 30 months.
- Patient was very compliant with at home care and all appointments throughout the study

Institutional review board statement

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Review Board of the Institute of Regenerative and Cellular Medicine (protocol code IRCM-2022-311 and approved on 12 January 2022).

Results

For both patients, wound diameter decreased from the initial allograft application to the final application shown in Table 1 and 2. Both had the total thickness of skin and tissue loss, visible tunnels, bone, and tendon were showing, classifying the wound as Stage IV. The most noticeable components of healing being granulation and epithelization, with no tunnels, tendon, or bone visible. Throughout the Wharton's jelly allograft applications, the epithelization of the SDU provided protection essential to mitigating wound infection and pathogens during the healing process. The application of Wharton's Jelly allografts was essential in augmenting the healing process of the SDU.

Table 1: Progression of length, width, and depth measurements in Patient 1 SDU over six applications of cryopreserved Wharton's jelly allograft.

Date of Application	Patient 1 SDU Measurement (LxWxD)	Dosage of WJ
1/5/2022	3.00 cm x 3.00 cm x 2.00 cm1	4cc
2/23/2022	2.00 cm x 1.00 cm x 1.60 cm	2cc
4/19/2022	1.20 cm x 1.20 cm x 2.10 cm2,3	2cc
5/31/2022	1.40 cm x 1.20 cm x 1.50cm4	2cc
8/23/2022	1.80 cm x 0.80 cm x 1.00 cm	2cc
9/13/2022	1.40cm x 0.80 cm x 0.60 cm	2cc
1/23/2023	1.00cm x 0.50 cm x 1.00 cm	2cc

Figure 1 Progression of the pressure sore for patient 1 a). Date of exam: 1 January 2022 b). Date of exam: 13 September 2022: c). Date of exam: 1 January 2023.

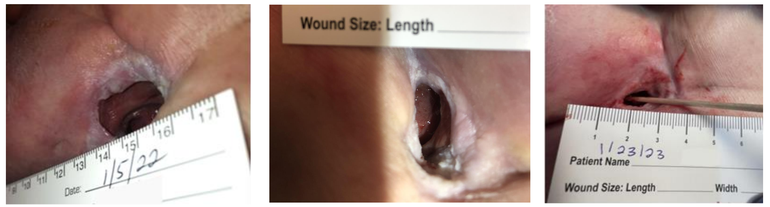

Figure 2 Progression of the pressure sore for patient 2 a). Date of exam: 16 December 2021; tunneling b). Date of exam: 15 March 2022; tunneling c). Date of exam: 23 August 2022; no tunneling, depth filled

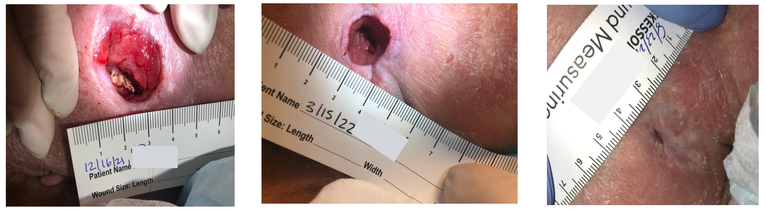

Table 2: Progression of length, width, and depth measurements in Patient 2 SDU over six applications of cryopreserved Wharton's jelly allograft.

Date of Application	Patient 2 SDU Measurement (LxWxD)	Dosage of WJ
12/16/2021	3.00 cm x 2.30 cm x 2.50 cm1	4cc
2/1/2022	1.20 cm x 1.50 cm x 1.50 cm2	2cc
3/23/2022	1.10 cm x 1.20 cm x 1.50 cm	2cc
4/13/2022	0.80 cm x 0.80 cm x 1.70 cm	2cc
5/17/22	1.10 cm x 1.10 cm x 1.40 cm3	2cc
8/23/22	1.60 cm x 0.10 cm x .8 cm	2cc
9/27/2022	2mm depth, 100% epithelialization	N/A

Conclusions

- WJ allografts accelerated wound closure, promoted granulation tissue formation, accelerated proper secondary intention wound healing, and diminished patient suffering and expenses.
- Both patient's avoided surgical intervention and had wound closure from deep to superficial.
- WJ allografts, along with standard of care treatment, present opportunity to reduce long-term morbidity and health care costs associated with decubitus ulcers.

References

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Materials and methods

All methods were completed in compliance with the FDA and American Association of Tissue Banks (AATB) standards.

Donation and Collection. Human umbilical cords were obtained from consenting mothers following full-term Cesarean section deliveries. An independent certified laboratory tested all donations for infectious disease in accordance with Clinical Laboratory Improvement Amendments (CLIA) of 1988, 42 CFR part 493, and FDA regulations. Each birth mother was tested for several bloodborne diseases. All test results were negative or non-reactive.

Preparation of Processed Umbilical Cord Tissue Samples Product. Wharton's jelly was aseptically dissociated from the rinsed umbilical cord. 100mg of Wharton's jelly was suspended in approximately 2mL of sterile Sodium Chloride 0.9% solution. The sample was not combined with cells, tissues, or articles other than the exceptions outlined in 21 CFR Part 1271.10(a)(3)

Allograft Application: Both patients received an initial Wharton's Jelly application of 4 cc or 200 mg of Umbilical Cord Tissue provided by Regenative Labs. The WJ was applied via a 25-gauge syringe in evenly radial increments. Five subsequent applications were given in the same manner, but the dose was reduced to 2 ccs or 100 mg. Patient one was seen every two to three weeks, and patient two was seen once a week in office. Due to Patient one's inconsistency with at home care and appointments , the study has been extended to provide extra WJ applications to achieve closure.

Discussion

- The present case study demonstrates that application of Wharton's jelly allografts significantly accelerate wound closure time.
- Patient 1 had a 94% decrease in wound volume, and patient 2 had a 100% decrease in wound volume. Both patients had failed at least 30 months of conservative and procedural management.
- That we are aware, these are the first case reports demonstrating substantial overall improvements in non-surgical wound closure where Wharton's Jelly allografts have been applied in tandem with standard of care wound treatments.
- The structure of collagen extracellular matrix fibers in WJ forms an architectural matrix homologous to ECM fibers in granulation tissue (8,9). Figures 3 and 4
- This case study provides a foundation for potential future research as both patients were at risk for sepsis, osteomyelitis, and further morbidity.

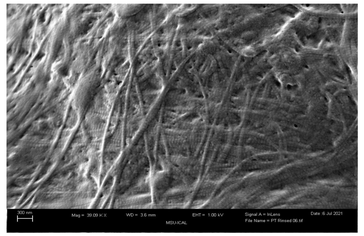

Figure 3. SEM micrographs of post-processed umbilical cord tissue samples. SEM image of preserved cross-linked collagen structures. (Scale bar: 300nm). Average fiber diameter, 65.4 nm.

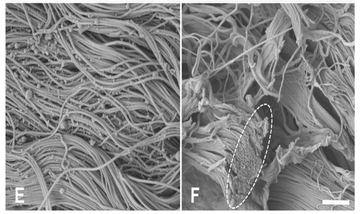

Figure 4. Scanning electron microscopy of native skin. In the higher 10,000x magnification type I collagen clotting was observed (interrupted circles) accompanied by a loss of cross-linking collagens. Scale bar 1 µm. The mean collagen fiber diameter from papillary and reticular dermis in normal skin was 56.2 +/- 2.5 nm and 62.8 +/- 4.3 nm respectively (8)

Acknowledgment

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