

SkinTE for the Treatment of a Complicated Wound after Synovial Sarcoma Resection: A Case Report

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Summary: Radiation therapy following oncologic resection can result in incisional breakdown, delay or cessation of wound healing, and exposure of structures. Impaired wound healing often mandates free tissue transfer for definitive closure and preservation of function. We present the case of a 16-year-old male patient who had a major incisional dehiscence following resection of a synovial sarcoma of the lower leg after postoperative irradiation. The progressive wound breakdown failed to respond to local wound care or negative pressure therapy and progressed to expose tendons of the distal leg. The patient was successfully treated with SkinTE, an autologous homologous skin graft and casting. Healing was slow but the wound filled with granulation tissue (which covered the tendon), epithelialized, and led to an excellent cosmetic and functional result. This highlights the potential of stem cell therapy and other forms of regenerative methods in healing of complicated wounds. (*Plast Reconstr Surg Glob Open* 2021;9:e3764; doi: 10.1097/GOX.0000000000003764; Published online 23 August 2021.)

Synovial sarcoma is a rare, malignant soft-tissue neoplasm commonly found around the joints and affecting predominantly teenagers and young adults. Treatment involves wide resection of the tumor with adjuvant doxorubicin or radiation therapy,¹ which severely impedes normal wound healing.² Radiation damage of tissues adjacent to a surgical incision can lead to dehiscence, infection, and exposure of deep structure including muscle, tendon, bone, and joints. Management of such wounds often necessitate autologous free tissue transfer to accelerate healing, limit infection risk, and minimize aberrant scarring mechanisms.³ Although other alternatives have been reported, the success rates are marginal and unpredictable.

This report describes successful closure of a large irradiated, nonhealing surgical wound of the distal third of the lower leg using SkinTE (PolarityTE, Inc. Salt Lake City, Utah), an autologous homologous skin construct (AHSC). The wound had progressed, enlarged, and

deepened despite vigorous local wound care and negative pressure therapy.

CASE REPORT

A 16-year-old, otherwise healthy teenage boy was evaluated in our clinic with intermittent medial left lower extremity pain and a barely palpable mass proximal to the left medial malleolus. Magnetic resonance imaging revealed a mass most consistent with neurofibroma, and surgical excision of a 3 × 2 × 2 cm mass was performed. The mass was friable and flesh-colored, and histology was read as synovial sarcoma with a positive SS18 cytogenetic rearrangement (SYT; 18q11.2) and positive margins. Whole-body PET scan, chest CT, and magnetic resonance imaging revealed no evidence of metastatic disease, and clear margins were obtained on a subsequent wide surgical excision keeping 1 cm margins of normal skin around the suture line. Aggressive adjuvant radiation therapy was completed over 3 months and the initially healed surgical incision gradually opened. Daily local wound management over a period of 2 months yielded no improvement, and the wound continued to widen and deepen to expose the posterior tibial tendon.

The wound was surgically debrided to visibly bleeding tissue and a negative pressure dressing was applied. After 10 days, the 15 cm × 6 cm wound had no active healing and no evidence of granulation over or around the exposed tendon (Fig. 1). Free tissue transfer was discussed with the family, but they wished to pursue other

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Fig. 1. Wound in the left lower extremity 10 days after debridement and application of negative pressure dressing, showing posterior tibial tendon exposure and little active healing or granulation of the wound bed.

options. SkinTE AHSC was proposed as an option and a 3 × 1 inch skin biopsy was obtained from the groin crease, packed in a sterile, temperature-controlled container, and sent for processing. Once processed and returned, the SkinTE AHSC substrate (which had the consistency of toothpaste) was applied to the clean wound base five days later and the protective silicone layer was stapled around the edge. A windowed short-leg fiberglass cast was placed to limit motion of the ankle. Gauze dressing was placed over the silicone and changed two to three times daily.

The wound was inspected weekly; the exudative drainage was pronounced for the first 2 weeks and the odor was challenging. The patient's wound was inspected under anesthesia 10 days after placement of the substrate, and a clear gel-like substance had covered the tendon and the wound bed appeared very clean and vascular (Fig. 2). Subsequent wound checks were done under anesthesia every two to three weeks to monitor wound progression. After 10 weeks, there was a sufficient coverage of the tendon and wound bed and the cast and silicone covering were permanently discontinued (Fig. 3). The patient continued daily dressing changes at home and kept the wound moisturized. Eight months after initial intraoperative SkinTE placement, the wound was fully healed with complete dermal coverage. Full-range motion of the



Fig. 2. Wound 10 days after placement of the substrate. The clear gel-like substance observed covering the tendon was adherent and firm; note granulation tissue entering superior edge over tendon.



Fig. 3. Wound after 10 weeks of treatment; robust granulation tissue with complete coverage of the tendon is observed.

affected lower extremity was also achieved, and the patient resumed normal activities. The patient has not presented any complications, and 14 months after surgery the wound is still fully healed with no necessity of additional treatment (Fig. 4).



Fig. 4. A 14-month follow-up after SkinTE placement with a fully healed wound and complete dermal coverage.

DISCUSSION

The wound healing progress observed in this case defied conventional paradigms. The radiated wound bed, which deteriorated with local wound care and was unresponsive to negative pressure therapy, showed a dramatic reversal after the application of SkinTE. While the process was protracted, the wound completely filled with granulation tissue, completely covered the exposed tendon, and epithelialized. Although the follow-up was work and time intensive, the wound healed with no adjuvant care or additional intervention besides managing the initial large exudative discharge. Overall, the AHSC-managed tissue achieved complete wound closure and functionality.

The functional pathways by which stem cells stimulate tissue regeneration are still not fully understood. Expanded potential stem cells (EpSCs) are multipotent adult stem cells present in the skin capable of self-renewal and differentiation into several cell lineages. Robust activation of EpSCs and efficient recruitment of their progeny towards an epidermal lineage has been shown to be critical for the re-epithelialization process.⁴ Given their valuable singularities, multipotent adult stem cells are an attractive choice for cell therapy due to their large proliferative potential, ability to differentiate into different cell types, and production of cytokines and trophic factors necessary for wound healing.⁴

AHSCs constitute a novel type of skin graft synthesized from the patient's own healthy tissue, where a small 3 × 1 inch full-thickness skin harvest is taken, allowing for minimal donor site morbidity.⁵ The tissue processing retains the EpSCs and supportive cells through generation of microaggregates and a physiologic media devoid of enzymes is then used to optimize passive diffusion and initiate skin repair. The AHSC is applied to the wound similar to a traditional autologous skin graft. The native wound bed will interact with the implanted autologous aggregate and expand within the wound, generating growing neo-dermal islands that close the wound from the inside out.^{5,6} This process was observed in our patient only after the wound bed had filled with healthy granulation tissue. Thus, the EpSCs appeared to not only alter the wound bed characteristics (ie, repel exudative build-up, robust granulation) but also exert some temporal control over the sequence of the wound healing processes. The functionally polarized EpSCs have been shown to stimulate full-thickness regeneration of the skin, hair follicles, and glands in the correct layers.⁷ AHSCs use the body's endogenous repair system and, in contrast to cells produced in tissue culture, are thought to not alter gene expression or cell behavior.⁵ Reports of successful wound management using AHSC have been described in the literature.^{6,8} However, the severely affected wound bed in our patient makes this among the worst cases successfully managed with this treatment, and highlights the potential of this stem cell therapy in tissue regeneration.

Potential limitations of using SkinTE for wound treatment must be acknowledged. These include its high cost and long duration of the healing process. While other alternatives could compensate for these disadvantages, a less time-consuming approach—such as a free flap—would have implied greater risks in our case due to the patient's previous exposure to radiation which affected

adequate vascularization of the affected tissue. Regarding wound healing costs, Samsell et al⁹ compared cost-effectiveness among several skin-substitute products in the management of diabetic foot ulcers. Products, such as DermACELL (D, LifeNet Health; Virginia Beach, Va.), EpiFix (EF, MiMedx; Marietta, Ga.), and Integra Dermal Regeneration Template (IDRT, Integra LifeSciences; Plainsboro, N.J.), among others, were studied. Results showed product costs per application and per treated wound, ranging from \$115 to \$1360, and \$1167 to \$3400 among the different products, respectively. For example, Integra DRT had a product cost per application of \$901.01, but a cost per treated wound of \$1802.02.⁹ This article was used as reference and analyzed by PolarityTE Inc.—the SkinTE manufacturer company—to compare SkinTE costs with these skin-substitute alternatives. The interim analysis revealed that SkinTE cost was 61% lower than the mean cost of product per treated wound reported by Samsell et al,⁹ with a mean total cost of around \$1300;¹⁰ however, costs may vary depending on the wound size and location. Further research is warranted to explore the potential for successful wound healing using AHSCs in other types of patients.

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