Histologically, there was a marked decrease in inflammatory infiltrate and a paucity of multinucleated giant cells, as compared with pretreatment biopsies.[4] In the treatment of rheumatoid nodules, another granulomatous condition, results have been mixed, and well-designed studies are lacking.[5]

The mechanism by which 5-FU works to resolve granulomas is not established, but the authors feel likely represents a combination of antiproliferative effects on immune cells, inhibition of fibroblast proliferation and collagen production, and resulting induction of tissue atrophy. Long-term controlled studies are necessary to further evaluate the efficacy and potential complications of the use of intralesional 5-FU in the management of cutaneous sarcoidosis.

References

1. Doherty CB, Rosen T. Evidence-based therapy for cutaneous sarcoidosis. Drugs 2008;68:1361–83.
2. Good LM, Miller MD, High WA. Intralesional agents in the management of cutaneous malignancy: a review. J Am Acad Dermatol 2011;64:413–22.
3. Lemperle G, Gauthier-Hazan N. Foreign body granulomas after all injectable dermal fillers: part 2. Treatment options. Plast Reconstr Surg 2009;123:1864–7.
4. Wiest LG, Stolz W, Schroeder JA. Electron microscopic documentation of late changes in permanent fillers and clinical management of granulomas in affected patients. Dermatol Surg 2009; 35:1681–8.
5. Diniz MS, Almeida LM, Machado-Pinto J, et al. Rheumatoid nodules: evaluation of the therapeutic response to intralesional fluorouracil and triamcinolone. An Bras Dermatol 2011;86: 1236–8.

Nima Gharavi, MD, PhD
Joseph Diehl, MD
Teresa Soriano, MD
Division of Dermatology
University of California
Los Angeles, California

The authors have indicated no significant interest with commercial supporters.

Healing of Recalcitrant Chronic Venous Leg Ulcers by Punch Grafts Harvested From the Scalp

Chronic venous leg ulcers (CVLE) represent an important therapeutic challenge because of their high prevalence, the high health service costs involved, and the impact on patient quality of life. First-line therapies of CVLE include compression therapy and wound dressings; however, despite these remedies, some ulcers remain unhealed. For difficult-to-heal ulcers, skin grafting has been used to promote healing.[1] These include autografts (pinch grafts, split-thickness skin grafts, and punch grafts), allografts, and tissue-engineered products.

Punch grafting for CVLE is a surgical technique that has been used for decades and can be performed in an ambulatory setting with minimal morbidity. The grafts have always been harvested from the thigh or the buttocks. Only one pilot study has reported the feasibility, safety, and promising results of transplanting hair graft harvested from the scalp into the wound bed of chronic leg ulcers.[2] The rationale for using grafts from the scalp instead of the traditional skin grafts harvested from less hairy areas such as the thighs or buttocks is based on the numerous research studies and clinical evidence indicating the wound healing–promoting effects of the hair follicles.[3]

The authors report 2 patients with CVLEs in which half of the ulcer area was transplanted with full-thickness punch grafts obtained from a nonhairy area and the other half from the scalp. The results confirm that graft punches containing terminal hair follicles heal better than nonhairy punches, representing a promising successful therapeutic alternative for nonhealing chronic wounds.

A 66-year-old woman with history of obesity and venous insufficiency presented with a painful ulcer (total area, 56.9 cm^2) on her right leg of 4-year duration that did not respond to conventional topical medications. In an outpatient setting, the authors decided to transplant autologous skin grafts in her ulcer, which was divided into 2 halves, one receiving hair grafts harvested from the scalp and the other half

receiving skin grafts from hairless abdominal skin (Figure 1). The scalp donor area was shaved before harvesting. Both donor areas and the ulcer wound bed were locally anesthetized with lidocaine 1% and epinephrine 1/100,000. The grafts were harvested using a 2-mm punch taking care to introduce the punch parallel to the scalp hair follicles to minimize follicular transection. The residual circular wounds in these donor areas were left to heal by second intention. The grafts were placed into a saline solution and immediately inserted into the ulcer wound bed using the so-called "stick and place" method,[2] which consists in the creation of a slit with a needle and at the same time the insertion of the graft into the slit with a fine-tipped forceps. The slits were made with a 14-gauge needle to accommodate the size of the graft. Once the grafts were inserted into the wound bed, the whole ulcer was covered with Vaseline gauze and an elastic bandage for 72 hours. After the intervention, the wound care applied to the ulcer was performed twice weekly, consisting in cleaning with saline and coverage with Vaseline dressing. At each follow-up visit after the procedure, the total area of the ulcer was measured using ImageJ software (National Institute of Health, Bethesda, MD). At Week 18 postgrafting, the half that received the scalp skin punches had fully healed, whereas the area that received abdominal skin grafts had decreased in size (13.53 cm^2) but had not completely epithelialized (Figure 2).

Figure 2. Patient 1: at Week 18 postgrafting, the half that received the scalp grafts had fully healed.

Another 64-year-old woman with history of venous insufficiency presented an ulcer of 5.25 cm^2 on the dorsum of her right leg of 2-year duration. She had not responded to topical medications, and the authors proceeded to perform the punch grafting technique. The surgical procedure was identical to that for the previous patient: one half of the ulcer was transplanted with 2-mm punch grafts harvested from the hairy scalp, and the other half with nonhairy punches from the abdominal skin (Figure 3). At Week 11 postintervention, the scalp punch side had almost totally healed, although there had been no significant reduction in the affected area receiving abdominal skin grafts (Figure 4).

Figure 1. Patient 1: scalp punch grafts transplanted into the lower half of the ulcer and abdominal skin punch grafts transplanted into the upper half.

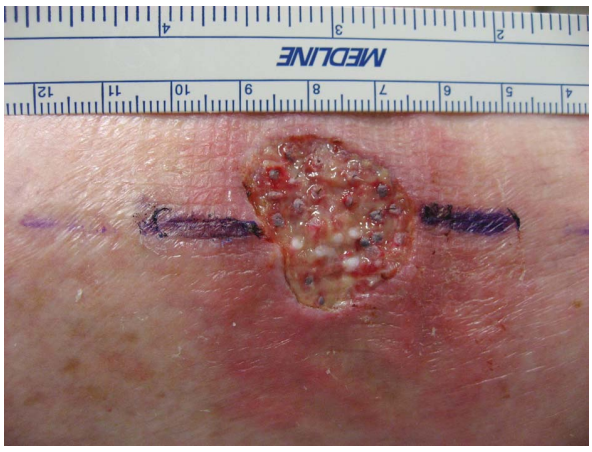

Figure 3. Patient 2: scalp punch grafts transplanted into the upper half of the ulcer and abdominal skin grafts transplanted into the lower half.

Figure 4. Patient 2: at Week 11 postintervention, the scalp grafted side was almost totally healed.

Discussion

Clinicians have observed for a long time that the healing of skin wounds starts around the hair follicles and that wounds made in hairy skin areas heal faster than those in nonhairy skin. This wound healing–promoting capacity of the hair follicle has also been reported. It seems clear that the hair follicle is the main repository of cutaneous stem cells, that bulge epithelial stem cells are recruited on wounding to help reepithelialize the skin, and that perifollicular mesenchymal cells can contribute to the dermal wound healing repair.[4] Therefore, if punch skin grafts can aid in healing chronic wounds, it would make more sense to harvest those grafts from areas such as the scalp with a high density of anagen terminal hairs, where the pool of follicular epithelial and mesenchymal stem cells with high proliferative, differentiating, and regenerative capacity is maximum.

In the 2 patients, the half of the ulcer that was transplanted with punch grafts harvested from the hairy scalp experienced a greater reduction in the ulcer area than the half transplanted with nonhairy grafts, confirming observations reported in a previous pilot clinical study.[2]

Besides the better healing results, the surgical technique of harvesting grafts from the scalp provides additional advantages: (1) the scalp 2 mm residual circular wounds heal very fast (in 5–7 days), leaving minimal pinpoint scarring that becomes totally unnoticeable[5] and (2) the process of graft implantation is technically easier because the stiffness of the scalp graft (because of the anagen terminal hair follicles) facilitates insertion into the wound bed of the ulcer.

In conclusion, the transplantation of scalp punch grafts is a minimally invasive surgical procedure that seems to be a useful therapeutic tool for CVLEs. More clinical reports and, ideally, randomized controlled studies need to be performed to be able to draw definite conclusions regarding comparative cost-effectiveness with other therapies. In addition, its usefulness in other nonvenous chronic ulcers needs to be investigated.

References

1. Jones JE, Nelson EA, Al-Hity A. Skin grafting for venous leg ulcers. Cochrane Database Syst Rev 2013;1:CD001737.
2. Jiménez F, Garde C, Poblet E, et al. A pilot clinical study of hair grafting in chronic leg ulcers. Wound Repair Regen 2012;20:806–14.
3. Jimenez F, Poblet E, Izeta A. Reflections on how wound healing-promoting effects of the hair follicle can be translated into clinical practice. Exp Dermatol 2015;24:91–4.
4. Jahoda CA, Reynolds AJ. Hair follicle dermal sheath cells: unsung participants in wound healing. Lancet 2001;358:1445–8.
5. Weyandt GH, Bauer B, Berens N, Hamm H, Broecker EB. Split-skin grafting from the scalp: the hidden advantage. Dermatol Surg 2009;35:1873–9.

María Luisa Martínez Martínez, MD
Dermatology Service
General Hospital of Villarrobledo
Albacete, Spain

Eduardo Escario Travesedo, MD
Dermatology Service
University General Hospital of Albacete
Albacete, Spain

Francisco Jiménez Acosta, MD
Mediteknia Dermatology and Hair Transplant Clinic
Medical Pathology Group
University of Las Palmas Gran Canaria
Canary Islands, Spain

The authors have indicated no significant interest with commercial supporters.