Pulsed-Dye Laser Treatment of Nonhealing Chronic Ulcer With Hypergranulation Tissue

Steven Q. Wang, MD; Leonard H. Goldberg, MD, FRCP; DermSurgery Associates, Houston, Tex; Dr Wang is now with the Division of Dermatology, Memorial Sloan-Kettering Cancer Center, New York, NY

The Cutting Edge: Challenges in Medical and Surgical Therapeutics

Second intention may be the best option available to the surgeon for the healing of particular surgical defects after Mohs micrographic surgery. It often provides satisfactory cosmetic and functional outcomes. However, healing takes longer than that for other repair options, and patients may need to endure a prolonged and cumbersome course of postoperative wound care. Some healing defects may develop hypergranulation tissue and become chronic ulcers especially.

REPORT OF CASES

CASE 1

An 82-year-old white man underwent Mohs micrographic surgery for treatment of a squamous cell carcinoma on the left side of his forehead in September 2002. The tumor was completely excised in 4 stages. The resultant 7.2 × 7.0-cm partial-thickness defect was allowed to heal by second intention. Initially, the wound care treatment consisted of biweekly wound cleansing with isotonic sodium chloride solution and dressing change with Aquaphor ointment (Beiersdorf Inc, Wilton, Conn), Telfa pads (Kendall, Mansfield, Mass), and Hypafix tape (BSN Medical Inc, Charlotte, NC). Although there was reepithelialization at the periphery of the defect after a 6-month period, the central portion of the wound had areas of persistent nonhealing ulceration and hypergranulation tissue. The area of ulceration and hypergranulation did not respond to treatment with fluocinonide ointment, 0.05%, under occlusion; repeated chemical debridement with trichloracetic acid, 35%; Protopic ointment, 0.1% (Astellas Pharma US Inc, Deerfield, Ill); or a 3-month trial with becaplermin gel. This situation did not change significantly for 3 years.

On September 29, 2005, 3 oval-shaped ulcerations with hypergranulation tissue were still present on the left side of the patient's forehead (Figure 1A). The epidermal border had a yellow, thickened scale but no drainage or signs of infection. The patient had no symptoms of pain or discomfort.

CASE 2

A 57-year-old white man underwent a 3-stage Mohs micrographic excision for a basal cell carcinoma on his right superior temple and scalp in August 2005. The resultant defect was 7.5 × 14 cm. The deepest portion of the defect extended to the loose fascia above the periosseum. The anterior portion of the defect involving the lateral canthus was repaired with a 7.0 × 4.0-cm full-thickness skin graft harvested from the patient's upper right arm. The posterior portion of the defect was allowed to heal by second intention. For the next 2 months, the wound was soaked and cleaned biweekly with isotonic sodium chloride solution and dressed with Aquaphor ointment (Beiersdorf Inc), Telfa pads (Kendall), and Hypafix tape (BSN Medical Inc). Later, the Aquaphor ointment was changed to fluocinonide ointment, 0.05%.

Two months after the surgery, the anterior portion of the surgical defect was covered by the skin graft. The posterior portion of the defect showed no signs of reepithelialization, and the entire area (approximately 8 × 7.5 cm) was filled with hypergranulation tissue rising 2 to 4 mm above the epidermal level. The patient had no significant discomfort or pain.

THERAPEUTIC CHALLENGE

Our challenge was to treat these patients, who had developed nonhealing chronic ulcers with hypergranulation tissue (CUHGT) after undergoing Mohs micrographic surgery on the scalp. The first patient, an elderly man, had failed multiple treatments over a 3-year period. The second patient also had developed exuberant granulation tissue that prevented epithelialization after undergoing Mohs surgery on his temple and scalp. Although numerous treatments for this condition have been tried, none has demonstrated clear efficacy. Patients often fail multiple treatments for CUHGT and struggle for a long time with large, open, nonhealing ulcers.

SOLUTION

In case 1, the hypergranulation tissue within the scalp ulcer was treated with a 595-nm pulsed-dye laser (PDL) (V-beam; Candela Corp, Wayland, Mass). The laser parameters were set at a fluence of 7.5 J/cm², a pulse duration of 3 milliseconds, and a spot size of 10 mm in diameter, and the dynamic cooling device was set at 30
milliseonds of cryogen spray with a delay of 30 milliseconds before the laser pulse. The entire ulcerated area was treated with double stacked pulses. Mild transient purpura was noted immediately after the treatment. The patient tolerated the procedure well. No local anesthetics were used because the hypergranulation tissue lacks nerve sensation. The patient was instructed to continue with the biweekly topical application of fluocinonide ointment, 0.05%, and to cover the wound with Telfa pads (Kendall) and Hypafix tape (BSN Medical Inc). After 6 weeks, the entire area had reepithelialized (Figure 1B).

Noticing the dramatic improvement in the first patient, we used the same 595-nm PDL on the second patient. Owing to the larger defect size and elevation of the granulation tissue, a more purpuric laser setting was used: a fluence of 11.5 J/cm², pulse duration of 3 milliseconds, a spot size of 7 mm in diameter, and the dynamic cooling device was set at 30 milliseconds of cryogen spray with a delay of 30 milliseconds before the laser pulse. Internal control testing efficacy of the PDL was used in this case: only the anterior half of the ulcerated defect was treated with the PDL. The treated area was single pulsed with a 50% overlap, and a nontransient purpura was seen immediately after the laser treatment (Figure 2A). The patient was instructed to apply fluocinonide ointment, 0.05%, and to cover the area with a Telfa pad (Kendall). Dramatic improvement was noticed, and a second treatment was administered 1 week later. Figure 2B shows the outcome 1 week after the second laser treatment. There was a dramatic flattening of the hypergranulation tissue and nearly 75% reepithelialization in the treated area. The untreated area shows no significant change or reepithelialization. One last PDL treatment was completed 1 week after the second laser treatment. The treated area achieved complete reepithelialization 5 weeks after the first PDL treatment, and the untreated area eventually reepithelialized 5 weeks after that. Figure 2C shows the complete reepithelialization of the entire defect.

**COMMENT**

The clinical problem of CUHGT is not uncommon following Mohs surgery of the scalp in which the postoperative defect is left to heal by second intention. It may also result from a variety of underlying medical conditions, such as stasis ulcer, diabetic ulcer, and nonhealing wounds after endotracheal intubation, gastrostomy tube placement, and a variety of dermatologic surgeries. Very little is known about the etiology, pathophysiologic characteristics, and treatment for hypergranulation tissue. Perhaps for this reason, there is an array of treatment modalities ranging from a simple polyurethane form dressing to aggressive surgical or chemical debridement. Yet, none of these treatment options is reliably curative.

Normal wound healing is a complex and well-orchestrated process. Disarray or aberrant development leads to poor or excessive wound healing. In the case of CUHGT, the exuberant dermal stoma tissue inhibits epithelialization and normal wound healing. Although the etiologies and mechanisms of hypergranulation formation are unclear, it seems that excessive angiogenesis may play a role. In the normal wound healing process, angiogenesis stops after the wound is filled with new granulation tissue. Many of the new blood vessels undergo apoptosis, and this programmed cell death may be triggered and regulated by thrombospondins 1 and 2, angiostatin, endostatin, and angiopoietin 2. In CUHGT, the wound bed is filled with numerous vessels, and apoptosis of the vessels does not occur. Furthermore, VEGF, a cytokine for inducing angiogenesis and vascular permeability, is significantly increased, as reported by Pokharel et al, who measured the VEGF messenger RNA and protein expression in 17 children who developed hypergranulation tissue after prolonged tracheotomy or endotracheal intubation. Lain and Carrington explored the antiangiogenic property of Aldara (3M, St Paul, Minn) and successfully treated a woman with a 6-cm diabetic ulcer on the plantar surface of the left foot.

We decided to target the superficial vessels in the hypergranulation tissue as the basis for our treatment initiative. For the 2 patients in our series, we used the 595-nm PDL, a laser commonly used for treating vascular lesions, erythema, pyogenic granuloma, and telangiectasias. The results seen in the 2 cases described herein were remarkable. The first patient had failed multiple treatments over a 3-year period, and then the scalp defect reepi-
Epithelialized after only 1 PDL treatment. The progress seen in the second patient was also remarkable, although not as dramatic. The PDL-treated area showed the 75% reepithelialization over a short (3-week) period. The untreated area showed no change. The internal control seen in this patient demonstrated the efficacy of PDL in treating CUHGT.

In summary, we present a novel use of PDL for the treatment of CUHGT. This laser treatment has been successfully used in 5 other patients with CUHGT and was well tolerated by all the patients. The clinical improvements in all patients were dramatic. The patients in our study had large post-Mohs surgical defects of the scalp that necessitated the use of second intention healing. It remains to be seen if PDL will be equally effective for treating CUHGT that resulted from other causes, such as diabetic ulcer or nonhealing wounds after endotracheal intubation and gastrostomy tube placements. Based on our case series, work by Lain and Carrington,” and the understanding of normal granulation tissue development, we hypothesize that excessive angiogenesis plays a major role in the formation of hypergranulation tissue. Targeting the vasculature of the hypergranulation tissue seems to be an effective therapeutic strategy for the treatment of CUHGT.

Accepted for Publication: July 4, 2006.

Correspondence: Leonard H. Goldberg, MD, FRCP, DermSurgery Associates, 7515 Main, Suite 240, Houston, TX 77030 (goldbl1@aol.com).

Author Contributions: Study concept and design: Wang and Goldberg. Acquisition of data: Wang and Goldberg. Analysis and interpretation of data: Wang and Goldberg. Drafting of the manuscript: Wang. Critical revision of the manuscript for important intellectual content: Wang and Goldberg. Administrative, technical, and material support: Wang and Goldberg. Study supervision: Wang and Goldberg.

Financial Disclosure: None reported.

REFERENCES