

BIDEAS AND INNOVATIONS Reconstructive

Treatment of Skin Avulsion Injuries with Basic Fibroblast Growth Factor

Hajime Matsumine, MD, PhD

Summary: This report describes favorable outcomes in 9 patients with skin avulsion injuries of the extremities who underwent full-thickness skin grafting and basic fibroblast growth factor (bFGF) application. Following removal of contaminated subcutaneous fat tissue on the inside of skin, the avulsed skin was processed into a full-thickness skin graft, with as much of the skin used as possible irrespective of damage. Several drainage holes (5– 10 mm in diameter) were made on the graft for drainage from the graft bed and to prevent seroma and hematoma formation. Genetically recombinant human bFGF was sprayed at a dose of 1 μ g/cm² onto the graft bed, which was then covered with the graft and sutured. Pressure immobilization with ointment gauzes and elastic bandages was administered for 1 week postoperatively, and the surface of the skin grafts that did not take was scraped away, preserving the revascularized dermal component on the debrided raw surface as much as possible. bFGF was sprayed again onto the debrided surface to promote epithelialization. Wound closure was achieved in all cases with conservative therapy. The surgical procedure was effective in preventing postoperative ulcer formation and scar contracture and resulted in wound healing with the formation of good-quality, flexible scars. (Plast Reconstr Surg Glob Open 2015;3:e371; doi: 10.1097/GOX.00000000000341; Published online 8 April 2015.)

number of surgical procedures have been reported as initial treatments for skin avulsion injuries of the extremities, including simultaneous skin grafting using the avulsed skin¹ and revascularization of the avulsed tissue under microscopy.² As this type of injury can occur at various sites and in various forms, the viability of avulsed skin can be difficult to evaluate, and in many cases, the avulsed

From the Department of Plastic and Reconstructive Surgery, Tokyo Women's Medical University, School of Medicine, Tokyo, Japan; and Institute of Advanced Biomedical Engineering and Science, Tokyo Women's Medical University, Tokyo, Japan.

Received for publication December 9, 2014; accepted February 26,2015.

Copyright © 2015 The Authors. Published by Wolters Kluwer Health, Inc. on behalf of The American Society of Plastic Surgeons. All rights reserved. This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives 3.0 License, where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially.

DOI: 10.1097/GOX.00000000000341

skin shows necrosis after initial surgery.³ Basic fibroblast growth factor (bFGF) dates back to 1974, when Gospodarowicz⁴ discovered a protein that promotes fibroblast growth from the bovine pituitary gland. This was followed by the development and commercialization of genetically engineered recombinant bFGF for the treatment of skin ulcer (Fiblast Spray; Kaken Pharmaceutical, Tokyo, Japan), which is clinically used in Japan. bFGF has been shown to be extremely useful for the treatment of skin ulcer,⁵ and its indications are expanding to include a combination therapy with artificial dermis⁶ and the treatment of second-degree burn injury.⁷ This report describes a surgical procedure using bFGF applied to a full-

Disclosure: The author has no financial interest to declare in relation to the content of this article. The FIBLAST Spray (Kaken Pharmaceutical, Tokyo, Japan) used in this study was purchased as a standard hospital supply by Tokyo Women's Medical University. The Article Processing Charge was paid for by Kaken Pharmaceutical. thickness skin graft for the treatment of skin avulsion injuries of the extremities.

MATERIALS AND METHODS

The present surgical technique was applied to skin avulsion injuries of the upper and lower extremities on the day of injury under general anesthesia. Avulsed skin in the wound was turned over while retaining its continuity, and the contaminated subcutaneous fat tissue on the inside of skin was removed with scissors from the distal to proximal ends of the skin. During fat tissue removal, bleeding from the subdermal vascular plexus was observed, indicating intact blood supply. After the avulsed skin was processed into a full-thickness skin graft, several drainage holes (5–10 mm in diameter) were made on the graft with a no. 11 scalpel for drainage from the graft bed and to prevent the formation of seroma and hematoma. The avulsed skin was used in its entirely whenever possible, regardless of the degree of damage. After the graft was immediately debrided, genetically recombinant human bFGF (100 µg/mL; Fiblast Spray) was sprayed at a dose of $1 \,\mu g/cm^2$ onto the graft bed. After 30 seconds, the graft bed was covered with the full-thickness skin graft and sutured. Postoperatively, pressure immobilization with ointment gauzes and elastic bandages was administered for 1 week. In addition, the surface areas of the skin graft that did not successfully take were scraped away carefully, preserving as much as possible the revascularized dermal component. bFGF was sprayed again onto the generated raw surface to promote epithelialization. Rehabilitation programs were gradually started 2 weeks postoperatively to prevent joint contracture.

CLINICAL CASES

The author applied the present surgical technique to skin avulsion injuries in 9 patients (age range, 8–65 years), including 5 patients with upper and 4 patients with lower extremity injuries. All patients were followed on an outpatient basis for 1 year postoperatively. After surgery, although the full-thickness skin grafts were partially ulcerated, the wounds healed with conservative therapy. There were no limitations in joint range of motion due to contracture, and cosmetic outcomes were favorable.



Fig. 1. Case 1: Intraoperative findings (A): Although the avulsed skin partly retained an attachment along the lateral aspect of the right foot, the skin was separated from the fascia of the muscle over a wide area. After removing contaminated subcutaneous tissue, a no. 11 scalpel was used to create multiple drainage holes through the avulsed skin. Following debridement of the contaminated tissue, basic fibroblast growth factor was sprayed over the graft bed and the graft bed was covered with the full-thickness skin graft. B, Postoperative findings at 6 months. The skin graft scar was flexible, soft, and without scar contracture or limitation in joint range of motion. Cosmetic outcome was favorable.

Matsumine • Treatment of Skin Avulsion Injuries with bFGF

Case 1

A 64-year-old man collided with a guardrail while operating a 2-wheel vehicle and suffered skin avulsion injury over the dorsum of the right foot. Surgery was performed on the day of the accident with present technique (Fig. 1A). Despite partial ulcer formation, the grafted skin healed with conservative treatment alone. Surgical outcome at 6 months postoperatively was excellent from a cosmetic standpoint, and range of joint motion was not limited due to contracture (Fig. 1B).

Case 2

A 37-year-old man had his right arm drawn into a roller machine and presented with skin avulsion injury of the right forearm. Surgery was performed on the day of the accident with present technique (Fig. 2A). Although edema formation extending distally from the skin avulsion injury was noted immediately after surgery, it gradually resolved after active rehabilitation started 2 weeks postoperatively. At 1 year postoperatively, the skin graft scar was flexible and soft with no scar contracture of the sutured wound and no limitation in the joint range of motion (Fig. 2B).

DISCUSSION

bFGF used in the present technique would have stimulated vascular endothelial cells and epidermal cells to promote angiogenesis, granulation tissue formation, and epithelialization,⁵ and bFGF was also recently shown to improve the quality of the scars formed as a result of epithelialization, by preventing hypertrophic scar formation and scar contracture.⁸ bFGF is considered to exert these effects by promoting (1) the proliferation of fibroblasts during the proliferation phase and (2) the apoptosis of fibroblasts and myofibroblasts, thereby decreasing their numbers during the reconstruction phase and preventing excessive wound constriction.⁹ Akita et al⁷ also reported that bFGF use in skin grafting for burn wounds resulted in the formation of a softer skin graft scar.¹⁰ The author has experience of treating injuries similar to those of the patients described here with a full-thickness skin graft prepared from the avulsed skin, but partial necrosis of the graft often occurred. In the present cases, the use of bFGF in combination with skin grafting improved both (1)the viability of the avulsed skin that was damaged to various degrees and (2) the quality of the skin and the marginal scar.

The intraoperative use of bFGF is expected to improve the engraftment rate of full-thickness skin grafts, reduce time to wound closure, bring forward the rehabilitation schedule, and prevent postop-



Fig. 2. Case 2: Intraoperative findings (A): The skin of the right forearm was avulsed circumferentially from the elbow to wrist, in some parts along with the fascia, with the continuity of the skin maintained only at the distal portion. The avulsed skin was turned over while retaining its continuity and was crushed from the distal to proximal ends of the skin. Contaminated subcutaneous fat tissue was removed with scissors, and the graft bed was covered with the full-thickness skin graft and sutured after spraying with basic fibroblast growth factor. B, Postoperative findings at 1 year. The skin graft scar was flexible and soft, with no scar contracture or limitation in joint range of motion. Cosmetic outcome was also favorable without pigmentation or decolorization.

erative motor dysfunction. The author previously reported that a bFGF drug delivery system greatly facilitated peripheral regeneration.¹¹ Although the recovery of sensory perception in the avulsed skin was not examined in the present study, the use of bFGF in skin avulsion injuries may facilitate the recovery of the neural networks in the damaged subcutaneous tissue.

CONCLUSION

Skin avulsion injuries of the extremities were treated with bFGF in combination with full-thickness skin grafting using the avulsed skin. The procedure was effective in preventing ulcer formation and scar contracture postoperatively and resulted in wound healing with the formation of a goodquality, flexible scar.

Hajime Matsumine, MD, PhD

Department of Plastic and Reconstructive Surgery Tokyo Women's Medical University 8-1 Kawada-cho, Shinjuku-ku Tokyo 162–8666, Japan E-mail: matsumine@diary.ocn.ne.jp

REFERENCES

- 1. Kudsk KA, Sheldon GF, Walton RL. Degloving injuries of the extremities and torso. *J Trauma*. 1981;21:835–839.
- Takeuchi M, Sasaki K, Nozaki M. Treatment of a degloved hand injury by arteriovenous anastomosis: a case report. *Ann Plast Surg*. 1997;39:174–177.
- 3. Jeng SF, Hsieh CH, Kuo YR, et al. Technical refinement in the management of circumferentially avulsed skin of the leg. *Plast Reconstr Surg.* 2004;114:1225–1227.
- 4. Gospodarowicz D. Localisation of a fibroblast growth factor and its effect alone and with hydrocortisone on 3T3 cell growth. *Nature* 1974;249:123–127.
- 5. Ono I. The effects of basic fibroblast growth factor (bFGF) on the breaking strength of acute incisional wounds. *J Dermatol Sci.* 2002;29:104–113.

- Akasaka Y, Ono I, Yamashita T, et al. Basic fibroblast growth factor promotes apoptosis and suppresses granulation tissue formation in acute incisional wounds. *J Pathol.* 2004;203:710–720.
- Akita S, Akino K, Imaizumi T, et al. A basic fibroblast growth factor improved the quality of skin grafting in burn patients. *Burns* 2005;31:855–858.
- 8. Fu X, Shen Z, Chen Y, et al. Recombinant bovine basic fibroblast growth factor accelerates wound healing in patients with burns, donor sites and chronic dermal ulcers. *Chin Med J (Engl).* 2000;113:367–371.
- 9. Muneuchi G, Suzuki S, Moriue T, et al. Combined treatment using artificial dermis and basic fibroblast growth factor (bFGF) for intractable fingertip ulcers caused by atypical burn injuries. *Burns* 2005;31:514–517.
- Gospodarowicz D, Ferrara N, Schweigerer L, et al. Structural characterization and biological functions of fibroblast growth factor. *Endocr Rev.* 1987;8: 95–114.
- 11. Matsumine H, Sasaki R, Tabata Y, et al. Facial nerve regeneration using basic fibroblast growth factor impregnated gelatin microspheres in a rat model. *J Tissue Eng Regen Med.* 2014 [Epub ahead of print].