

Case Report: Rapidly Healing Epidermolysis Bullosa Wound After Ablative Fractional Resurfacing

Andrew C. Krakowski, MD^{ab}, Pedram Ghasri, MD^c

Recessive dystrophic epidermolysis bullosa (RDEB) is a devastating genodermatosis characterized by generalized skin fragility, severe blistering, and wounding that heals with mutilating scarring. Patients are in constant need of effective wound therapies as they often succumb to aggressive metastatic squamous cell carcinomas or to sepsis that may develop from their chronic wounds. Herein, we demonstrate accelerated wound healing with use of a fractionated CO₂ laser protocol in a 22-year-old man with RDEB. His 9-month-old, non-healing wound decreased from 7 cm in diameter to 2 cm in diameter (a 92% reduction in wound surface area) within 4 weeks of a single laser treatment, and he had near-complete re-epithelialization within 4 weeks of his second laser treatment without blistering or other adverse effects. This novel intervention of using fractionated CO₂ for photo-microdebridement could help revolutionize wound care for patients who have RDEB and whose chronic wounds serve as one of their greatest sources of morbidity and mortality. Dissemination to a pediatric audience is critical so that laser protocols might be more thoroughly investigated and incorporated into wound management strategies for this uniquely vulnerable population.

The development of chronic wounds remains a significant cause of morbidity and mortality for patients who have recessive dystrophic epidermolysis bullosa (RDEB), an inherited condition characterized by generalized skin fragility, severe blistering, and wounding that heals with mutilating scarring. Patients are in need of effective wound therapies as they often succumb to aggressive metastatic squamous cell carcinomas (SCC) and to sepsis that may develop from their chronic wounds.

Ablative fractional laser resurfacing (AFR) is an emerging therapy for treating chronic wounds, having recently shown promise in the adult and pediatric populations.^{1,2} Herein we report marked, rapid improvement in a large chronic wound of a patient with RDEB after 2 treatments with a novel

ablative fractional laser resurfacing protocol.

CASE

A 22-year-old man with RDEB presented for evaluation of a large, “very painful,” non-healing wound on his left upper back that had been present for 9 months despite intensive RDEB wound care that included routine use of petrolatum-based ointment (Aquaphor ointment, Beiersdorf, Inc, Wilton, CT) and silver-impregnated foam dressings (Mepilex Ag, Mölnycke Health Care Inc, St Laurent, Quebec, Canada). Serial bacterial cultures taken from his numerous chronic wounds have demonstrated continued colonization with methicillin-sensitive *Staphylococcus aureus*, Group B *Streptococcus*, and *Pseudomonas aeruginosa*. Early in his life the patient

abstract

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Dr Krakowski conceptualized and designed the study, acquired data from patient interaction and procedures, reviewed and revised the manuscript, and provided final approval of version to be published; Dr Ghasri helped draft the initial manuscript and reviewed and revised the manuscript, and both authors approved the final manuscript as submitted.

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developed drug allergies requiring life sustaining interventions to vancomycin cross reactors and penicillin cross reactors; consequently, his medical team has attempted to judiciously reserve the use of systemic antibiotics to times of true infection only. Physical examination revealed a non-inflammatory ulcer measuring approximately 7 cm in diameter with friable granulation tissue present (Fig 1A). The ulceration had started as a small erosion that failed to respond to RDEB wound care protocols and grew larger with repetitive trauma. There were no signs of local infection. Against the advice of his medical team, the patient initially deferred a skin biopsy of the area to help rule out SCC; he was close to demoralized and was unwilling to endure any additional pain and the possibility of “just another hole in me that won’t heal.”

After obtaining informed consent, the ulceration and surrounding wound areas were treated using an ablative microfractionated 10 600-nm CO₂ laser (Ultrapulse Encore Deep FX, Lumenis, Ltd, Yokneam, Israel). Anesthesia was provided with topical lidocaine 4% cream applied under occlusion for 1 hour and was supplemented intraoperatively with ice only. The entire wound area was treated with a single pulse, nonoverlapping stamping technique at pulse energy of 30 mJ and treatment density of 5%. Conceptually, treatment density is decreased with increasing depth to prevent excessive thermal injury; a treatment density of 5% means that 95% of the wound surface remains untreated within the “stamped” square pattern (Fig 2). Immediately after AFR treatment, a petrolatum-based ointment was applied (Aquaphor ointment, Beiersdorf, Inc,

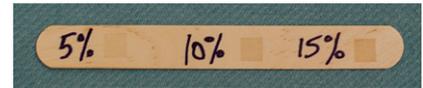


FIGURE 2
Tongue depressor after treatment with AFR depicting a “stamped” square pixelated pattern and demonstrating the difference between density settings of 5%, 10%, and 15%.

Wilton, CT) and continued 2 to 3 times a day. No postoperative complications were reported and the patient resumed his normal activities and wound care strategies 1 day after his treatment.

The patient returned in 4 weeks, and his ulcer measured approximately 2 cm in diameter; this represented approximately a 92% decrease in wound surface area (Fig 1B). Only “mild” discomfort was noted. A second treatment was performed using only topical anesthesia and the original treatment settings. Two weeks later, the patient provided photos via email to document his wound’s continued progress (Fig 1C). At a follow-up appointment 4 weeks after the second laser treatment, the patient’s wound demonstrated near-complete re-epithelialization (Fig 1D). He reported being “pain free” in the affected area. He also felt “happier” and “more excited” about participating in a novel treatment. Somewhat surprisingly, the patient consented to a punch biopsy of the now-healed wound area, explaining that he was more confident in the ability for his fragile skin to heal with AFR. Histopathologic examination revealed a mildly hyperkeratotic superficial epidermis with mild acanthosis and hypergranulosis; the epidermis was split from the underlying dermis at the edge of the biopsy, consistent with a subepidermal vesicle in the setting of RDEB. Rare eosinophils were present in the epidermis. The dermis was noted to be fibrotic and had several plasma cells with smaller numbers of eosinophils, lymphocytes, and histiocytes. Inflammation was predominantly in a perivascular

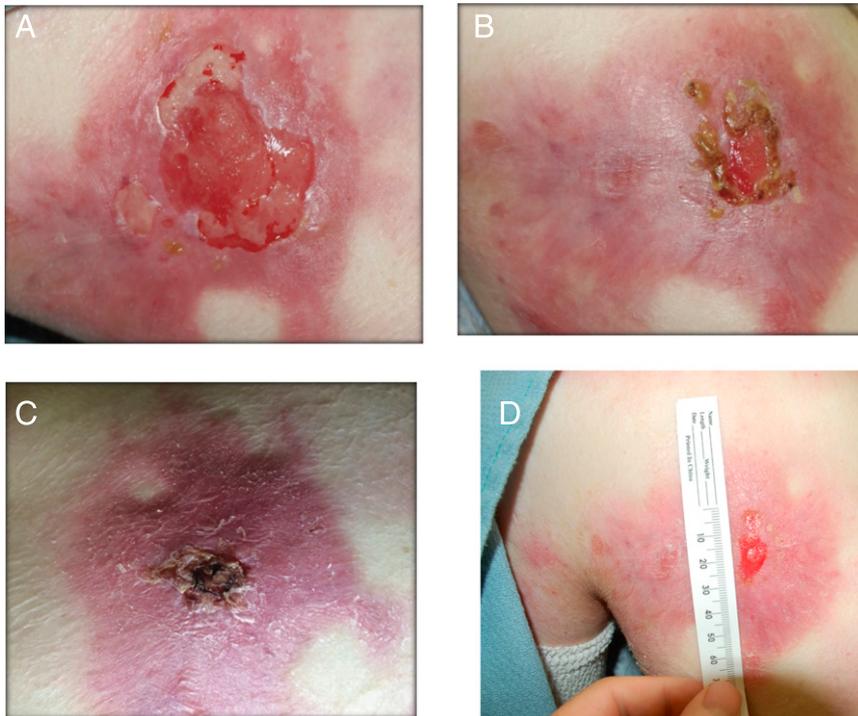


FIGURE 1
A, Non-healing ulcer measuring 7 cm in diameter present on patient’s left upper back for 9 months. B, Healing ulcer now 2 cm in diameter 4 weeks after first treatment with microfractionated CO₂ laser, representing a 92% reduction in wound surface area. Evident toward the “3 o’clock” position is a faint, square outline caused by AFR’s stamping technique. C, Continued progress of ulcer 2 weeks after second laser treatment. D, Near-complete re-epithelialization of chronic wound 4 weeks after second laser treatment; punch biopsy revealed no evidence of SCC.

distribution with some scattered inflammatory cells throughout the collagen in the upper dermis. No evidence of SCC (ie, atypia or proliferation) was seen. Based on the outcome of his left upper back wound, the patient opted to treat 2 smaller ulcerated wounds on his left anterior shin and right upper back via AFR; these wounds have since demonstrated similar clinical results.

DISCUSSION

Chronic wounds remain a significant cause of morbidity and mortality for patients with RDEB, an inherited genodermatosis characterized by mutations in the COL7A1 gene. This condition is defined by altered structure or disrupted production of type VII collagen, the main component of anchoring fibrils that help secure the epidermis to the dermis. Patients with RDEB demonstrate generalized skin fragility with friction or minor trauma leading to the formation of severe blisters that may present over the entire body. Corneal involvement can lead to erosions, scarring, and vision loss.³ Oral scarring may lead to ankyloglossia and progressive microstomia, and esophageal erosions may form strictures and webs with progressive dysphagia. Overall, severe nutritional deficiency often results.

Skin wounds in patients with RDEB are often chronically painful and may be a cause of tremendous stress, anxiety, depression, and drug dependence and abuse in older patients. Wounds are often complicated by secondary infection, and many patients become infected with resistant bacteria, including methicillin-resistant *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Blisters may heal with mutilating scarring with complications that include severe loss of function resulting from fusion of the fingers and toes (ie, "mitten" deformities of the hands and feet) and from contracture formation over joints.

In patients who survive the risk of sepsis in childhood, the most common cause of mortality is aggressive metastatic SCC. There is a >90% lifetime risk for patients with RDEB to develop SCC.⁴ These cancers usually appear between the second and third decades of life; however, any non-healing, atypical appearing wound, especially one with exuberant scar tissue, should raise suspicion for SCC.⁵ A fragment of collagen VII known as the amino-terminal non-collagenous domain has been established to be required for Ras-driven human epidermal tumorigenesis; it is hypothesized that retention of non-collagenous domain sequences could help explain the increased risk for SCC in RDEB.⁶

A 2009 systematic review of randomized controlled trials of treatments for inherited forms of epidermolysis bullosa revealed no reliable evidence for interventions. Study design, small samples, short treatment periods, and loss of patient sample were all cited as factors that have made the validation process difficult. The authors suggested that, in the future, gene treatment may become the best treatment approach for these conditions.⁷ Meanwhile, multidisciplinary prevention of clinical complications and local measures remain the only effective strategies to control associated morbidities. Traditional wound management strategies have included lancing and draining blisters to prevent further spread from fluid pressure, use of bandages and dressings, topical emollients/antibiotics, and surgical debridement.

The proposed mechanism of action of AFR in the accelerated healing of this large, chronic RDEB wound is most likely multifactorial. "Photo-microdebridement" of the local area may allow for the beneficial effects of traditional surgical debridement without the significant associated downtime.¹ Disruption of any local biofilm, collagen stimulation

(especially type 3 collagen), and secretion of growth factors from the adjacent intact dermis may also play key roles.⁸⁻¹⁰

It is possible that this patient's wound healing was not the result of intervention with AFR and that his outcome might be explained, in part or in whole, by other factors such as routine RDEB wound care, tincture of time, and change in his activity level. The dramatic improvement in this large wound that had been persistently present for 9 months despite intensive RDEB wound care, however, suggests that intervention with AFR played some role. Offering support to this theory is a 2012 prospective, randomized, double-blinded, placebo-controlled, crossover-designed trial that examined the use of trimethoprim to treat RDEB wounds. Although trimethoprim ultimately failed to achieve statistically significant results against placebo, the authors reported that only 2 of 6 subjects receiving placebo attained "more than 50% reduction in chronic wound area" over the 2-month study period.¹¹ Compared with these placebo subjects the clinical results achieved in our patient with RDEB whose wound was treated with AFR suggest superiority in both reduction in chronic wound area and time to resolution.

Although further studies are necessary to determine the true efficacy and safety of AFR in the RDEB population, this relatively noninvasive treatment of chronic wounds should be considered in patients who have failed or have contraindications to traditional RDEB treatment modalities. Likewise, the prospect of laser-assisted delivery of antimicrobial agents, antineoplastic therapies, wound healing growth factors, and "gene correction" applications through AFR's ablated microchannels could revolutionize overall RDEB management strategies.

EDITOR'S NOTE

Pediatrics publishes this case report cognizant of the patient and subject's age being 22 years (not in the pediatric age range). Recognizing that the morbidity of Epidermolysis Bullosa affects both pediatric and adult patients, it is hoped that this manuscript might act as a starting point for use and dialogue about the use of this treatment modality in the care of this disfiguring condition.

—Associate Editor J. Malatack

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