

RESIDENT COMPETITION RESEARCH ARTICLES

Improvement with Fractional Ablative Laser and Topical Poly-L-Lactic Acid in an RDEB Patient

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ABSTRACT

Recessive dystrophic epidermolysis bullosa (RDEB) results from mutations in the *COL7A1* gene for type VII collagen. Affected patients demonstrate skin fragility and blistering with scarring. Associated morbidity is great, and there are limited therapeutic options. Fractional carbon dioxide (CO₂) ablative laser (FABL) treatments have been shown to promote collagen remodeling and demonstrate synergy with topical poly-L-lactic acid (PLLA) applications. We report the case of a young woman with RDEB who experienced decreased blistering, decreased healing time, and improved quality of life in a local skin area treated with FABL followed by topical PLLA. In comparing biopsy specimens from treated and untreated skin, improved collagen organization and collagen maturity were observed by histopathological examination including with Herovici staining. Moreover, type VII collagen, absent in untreated skin, was detected in treated affected skin by immunostaining. This report illustrates a treatment response to FABL and topical PLLA in a patient with RDEB including enhanced healing time, collagen remodeling, and type VII collagen expression. The findings are promising and, with further study, may have broader implications for treating this disorder.

INTRODUCTION

Recessive dystrophic epidermolysis bullosa (RDEB) is an autosomal recessively inherited disorder resulting from mutations in *COL7A1* encoding type VII collagen, a basement membrane zone component. Patients with RDEB suffer from skin fragility with limited effective management therapies.

Fractional ablative laser (FABL) therapy improves scars through collagen

remodeling¹⁻⁴ and has accelerated wound healing in RDEB.⁵ Topical application of poly-L-lactic acid (PLLA) to scars after FABL improved outcomes.⁶ We report a patient with RDEB with long-standing chronic lesions who experienced clinical and immunohistopathologic improvement with combination FABL-topical PLLA treatments accompanied by overall patient satisfaction and improvement in quality of life.

CASE REPORT

A young woman with RDEB presented for large non-healing chronic erosions on her upper back and posterior neck (Figure 1A) that had been present for years. She had been using topical wound care treatments and oral antibiotics without significant improvement. Treatment with an ablative microfractionated 10,600-nm carbon dioxide laser/FABL (Ultrapulse Encore Deep FX; Lumenis, Ltd., Yokneam, Israel) was administered to an affected area with single pulse, nonoverlapping stamping technique (15mJ energy, 15% density). Immediately following FABL, 183.6 g of PLLA (Galderma, Fort Worth, TX) was applied topically to treated areas. Treatments were administered every six weeks on average for a total of fifteen treatments. The patient reported improvement in post-laser healing time, decreased skin fragility, fewer blisters, and overall decreased lesion size (Figure 1B) without other changes in her topical regimen. The patient healed in less than one week after six treatments compared to at least two weeks healing time after initial treatments. Intra-procedural bleeding markedly decreased as the number of treatments increased. She has had few to no blisters after completion of fifteen treatments and has maintained a decreased overall lesion size over two years.

After seven treatments, punch biopsies were obtained from treated affected skin (TAS), untreated affected skin (UAS), and clinically normal-appearing skin (NS). On hematoxylin-and-eosin (H&E) staining, TAS demonstrated scar-like fibrosis with chronic dermal inflammation. UAS showed detached epidermis overlying abnormal collagen organization with dermal fibrosis and chronic inflammation (Figures 2A and 2B). Herovici staining, which differentiates mature (type I)

from immature (type III) collagen, revealed an increased expression of type I collagen in TAS compared to UAS (Figures 2C and 2D). TAS, UAS and NS were evaluated by indirect immunofluorescence for type VII collagen expression. Type VII collagen was detected in TAS and resembled type VII collagen immunostaining in a normal human control, whereas type VII collagen immunostaining was not detected in UAS or NS (Figure 3).

Figure 1. Clinical images of the skin pre- and post-treatments.

Posterior neck of the patient with recessive dystrophic epidermolysis bullosa (RDEB) reported herein before (Figure 1A) and after (Figure 1B) fractional ablative laser (FABL) and topical poly-L-lactic acid (PLLA) treatments (dotted lines indicate treated area).



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Figure 2. Histopathology and immunostaining findings on skin biopsy specimens of untreated and treated affected skin and normal-appearing skin. Hematoxylin and eosin (H&E) staining of the untreated skin (Figure 2A) demonstrates a detached epidermis with dermal fibrosis and chronic inflammation; H&E staining of the treated skin (Figure 2B) shows scarring, fibrosis, and chronic dermal inflammation, with an intact epidermis demonstrating compact hyperkeratosis. Notably, with respect to collagen organization, the untreated skin demonstrated thick, jumbled collagen (Figure 2A), whereas the treated skin had finer collagen bundles with more definite “east-west” organization (Figure 2B). Herovici staining demonstrates more blue staining of immature type III collagen in untreated skin (Figure 2C) than in treated skin (Figure 2D), which demonstrates more pink staining indicating an increase in mature, type I collagen.

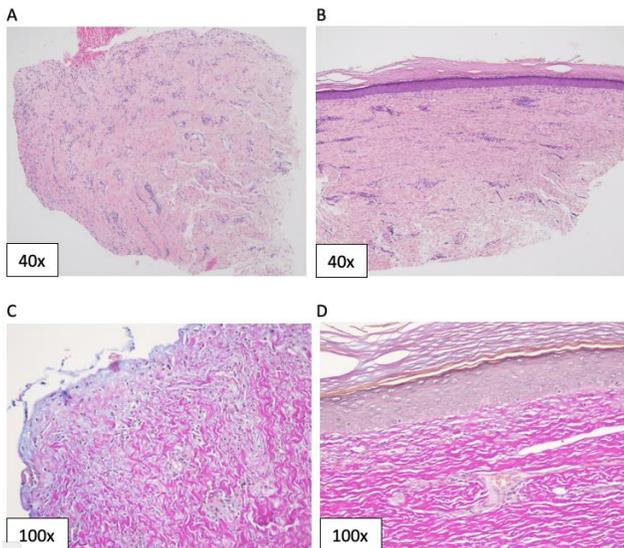
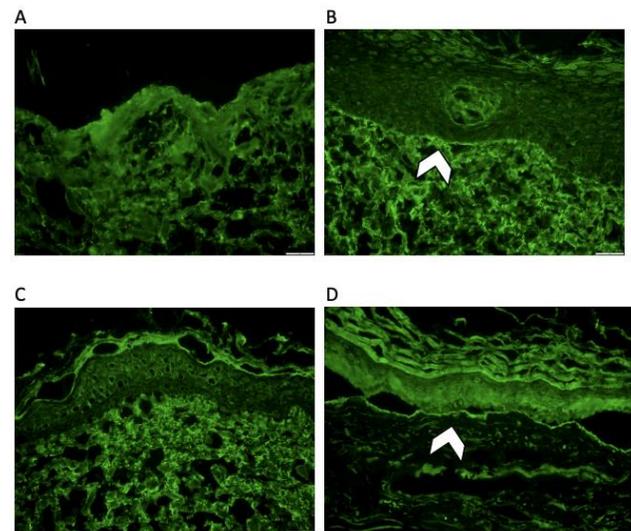


Figure 3. Immunofluorescence findings on skin biopsy specimens of untreated affected skin, treated affected skin, and clinically normal skin.

Indirect immunofluorescence testing for type VII collagen was performed on biopsy specimens from the patient’s untreated affected skin, treated affected skin, clinically normal-appearing/apparently unaffected skin, and normal cadaveric skin (as a positive control) using serum with known IgG collagen VII antibodies* as the primary antibody and fluorescein isothiocyanate-conjugated anti-human IgG as the secondary/detection antibody. No type VII collagen is detected in the untreated affected skin (Figure 3A) or in the clinically normal-appearing skin (Figure 3C); however, type VII collagen is detected in treated affected skin (Figure 3B) along the basement

membrane zone (BMZ), white arrowhead, suggesting that FABL and topical PLLA treatments may induce collagen VII expression. Normal cadaver skin (Figure 3D) demonstrates the normal BMZ collagen VII expression (white arrowhead).

*Serum from two patients with epidermolysis bullosa acquisita with dermal pattern IgG basement membrane zone antibodies on split skin substrate by indirect immunofluorescence and increased IgG collagen VII antibody level and normal IgG BP 180 and BP 230 antibody levels by ELISAs showed similar findings.



DISCUSSION

FABL induces collagen remodeling with improved scar texture and cosmesis resulting in improved quality of life due to decreased wound fragility and less visible lesions.¹⁻⁴ PLLA acts synergistically with FABL to mediate collagen remodeling.⁶ Three case reports describe the utility of laser therapy in epidermolysis bullosa patients^{5,7,8}; however, this is the first report, of which we are aware, of a patient treated with combination FABL-topical PLLA.

FABL likely stimulated healing of the affected area through mechanisms of microdebridement and neocollagenesis.⁹ Heat induced by FABL introduces miniscule channels into the epidermis and superficial

dermis serving as thermal microdebridement that affects inflammation and, ultimately, collagenesis. PLLA acts synergistically to induce neocollagenesis. In this model, the response to combination FABL-topical PLLA is quicker restoration of dermis with less aberrant collagen. This translated to faster healing times and more normal-appearing scar tissue with collagen VII expression on histopathology and immunostaining in the patient reported herein. Based on these promising findings, combination FABL-topical PLLA may be a therapeutic option for patients with RDEB who have exhausted conventional therapies.

Further studies are needed to establish this and to determine, as we theorize, whether this combination therapy may have broader applicability.

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