A case report of Hailey-Hailey disease treated with fractional carbon dioxide laser

Zivile Gabdrafike,[1,2] Monika Blazeviciute,[1,2] Ugne Janonyte,[1] Jurgita Makstiene,[3] Skaidra Valiukeviciene[1,2]

[1]Department of Skin and Venereal Diseases, Lithuanian University of Health Sciences, Medicine Academy, Kaunas; [2]Department of Skin and Venereal Diseases, Hospital of the Lithuanian University of Health Sciences, Kauno Klinikos, Kaunas; [3]Department of Pathology, Hospital of the Lithuanian University of Health Sciences, Kauno Klinikos, Kaunas, Lithuania

Abstract

Hailey-Hailey disease (HHD), or familial benign pemphigus, is a rare genetic condition characterized by recurrent blisters and erosions with a predilection for intertriginous areas. There is no specific treatment for HHD. Topical and systemic treatments tend to provide temporary remission. Alternative treatment (surgical interventions such as dermabrasion, excision, and laser) has been shown to prolong remission. Considering the risk of complications associated with surgical modalities, laser is often preferred as an alternative for patients failing to respond to first-line therapies. We report a case of recalcitrant HHD successfully treated with a fractional ablative CO_2 laser procedure (wavelength of 10600 nm, power of 7-10 W, 2-3 passes) on a 35-year-old female. The patient has a 7-year history of therapy-resistant HHD. A 2-month follow-up showed substantially resolved lesions, with mild erythema and post-inflammatory hyperpigmentation in treated areas.

Correspondence: Zivile Gabdrafike, Department of Skin and Venereal Diseases, Hospital of the Lithuanian University of Health Sciences, Kauno Klinikos, Eiveniu str. 2, LT-50161, Kaunas, Lithuania. E-mail: zivile.aukstakojyte@stud.lsmu.lt

Key words: Hailey-Hailey disease, familial pemphigus, laser therapy, carbon dioxide laser.

Contributions: ZG, MB, SV, JM, devised the work and its' conception; ZG, UJ, wrote the first draft of the manuscript and all authors commented and modified the previous versions. Each author has agreed to be personally accountable for their contribution and to ensure the accuracy or integrity of any part of the work. All authors read and approved the final version of the manuscript.

Conflict of interest: the authors declare no potential conflict of interest.

Patient consent for publication: written informed consent was obtained from the patient.

Funding: none.

Availability of data and material: data and materials are available by the authors.

Conference presentation: 18th Congress of the Baltic Association of Dermatovenerologists (BADV), September 22-24, 2022, Riga, Latvia.

Received: 27 December 2022.
Accepted: 10 January 2023.
Early view: 21 April 2023.

Dermatology Reports 2023; 15:9658
doi:10.4081/dr.2023.9658

Introduction

Hailey-Hailey disease (HHD) is a rare autosomal-dominant blistering dermatosis known as benign chronic familial pemphigus. It was first described in 1939 by the Hailey brothers.[1] Clinically, HHD usually tends to appear between the third and fourth decade, although the symptoms can occur at any age.[2] The disease is characterized by recurrent blisters that give rise to fissured plaques and macerations of the overlying epidermis, typically within intertriginous areas.[3] The recurrent pattern and chronic course of the disease pose a challenge for satisfactory treatment. Conventional medical intervention tends to include both local and systemic treatment, depending on the individual case. Alternative treatment options include surgical interventions such as dermabrasion, excision, and laser therapy.[4] We report a case of recalcitrant HHD successfully treated with a fractional carbon dioxide (CO_2) laser.

Case Report

A 35-year-old woman presented with a 7-year history of recurrent, therapy-resistant, histologically confirmed HHD (Figure 1). The patient was initially treated with topical clobetasol 0.05% once daily for 30 days with no lasting clinical effect. Thus, the treatment was altered: topical fucidin 2% cream for 14 days and betamethasone ointment 1% twice daily for 14 days were prescribed.The last exacerbation resulted in a widespread form of HHD with complaints of weeping sores and pruritus. A dermatological examination revealed erosions and multiple weeping sores of various sizes up to 0.5 mm deep on the chest and inframammary region. Erosions, plaques covered with scabs, and excoriations were also observed on the back, axilla, and interthoracic region. Serological blood tests for autoimmune bullous skin diseases (BP180, BP230, desmoglein I and III, envoplakin, antinuclear antibodies, collagen type VII antigens) were performed and found to be negative. Family history was non-contributory. Swab cultures obtained from the inframammary region revealed the growth of *Candida kefyr*, *Staphylococcus aureus*, and *b-hemolytic Streptococcus*. Initial local treatment

included octenisept and fibrosol dressings, octenisan wash lotion, and zinc oxide paste for rashes in the axilla region once daily. Systemic treatment consisted of cefazolin 1 g 4 times a day for 7 days and fluconazole 150 mg once daily for 5 days. During the course of the treatment, the skin condition improved slightly. However, a follow-up after a month showcased a progressing HHD. The rash on the chest and axilla region reappeared a week prior and was spreading (Figure 2). Treatment with tacrolimus 0.03% ointment twice daily, emollients 2/3 times a day, and antiseptics were prescribed. After 2 weeks, the secretion of the wound increased, followed by a burning sensation, and treatment with tacrolimus was discontinued.Bearing in mind the relapsing-remitting course, the severity of the disease, and the history of poor response to conventional treatment, the CO_2 laser procedure was performed on an outpatient basis using local anesthesia of 5% lidocaine. The laser system used was the MedArt® 620 FRx^{1M} (Hvidovre, Denmark) with the MedArt® 459 fractional scanner (Hvidovre, Denmark). Three passes on the 2×2 cm lesion in the left inframammary area with a power of 10 W were performed during the first session. Aftercare included zinc oxide paste and antiseptics twice daily, plus mepilex lite dressings. A follow-up after 4 weeks revealed no recurrence of the lesions in the treated area; only a pink plaque was left (Figure 3). A 2-month follow-up showed substantially resolved lesions, with mild erythema and post-inflammatory hyperpigmentation in treated areas. The patient reported a substantial improvement in quality of life and was highly satisfied with the treatment. Side effects included moderate postoperative pain (about a week), mild secretion from the treated lesion, and slight hyperpigmentation. A new recurrence within the treated site or scarring was not observed.

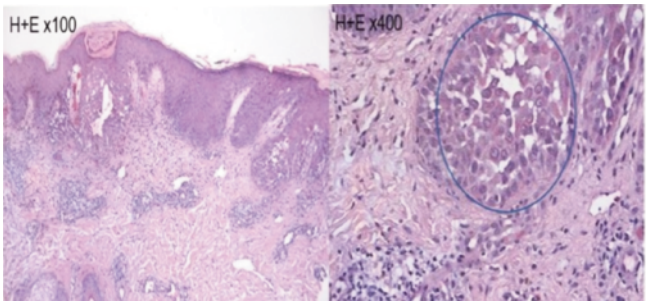

Figure 1. Epidermal acantholytic keratinocytes (blue circle).

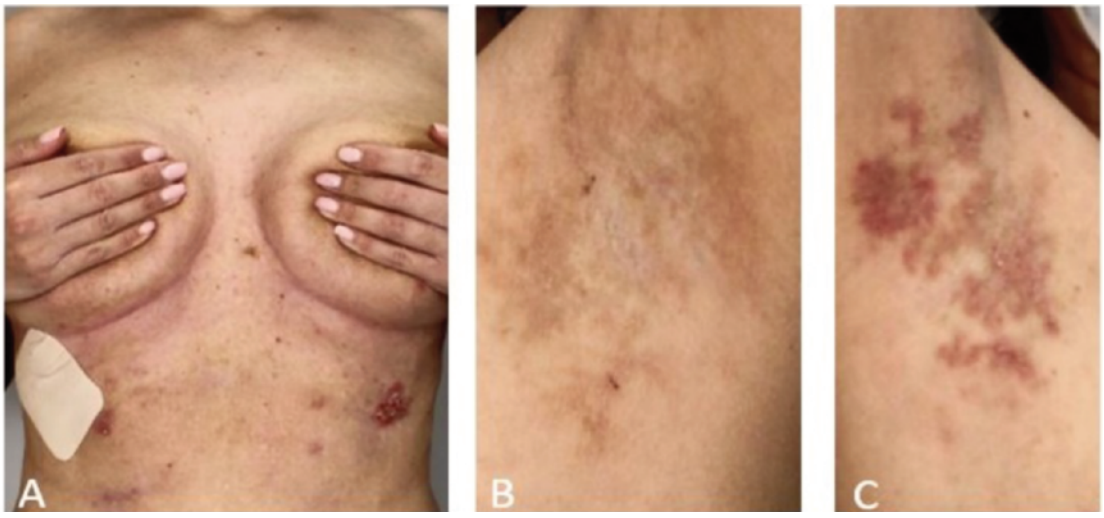

Figure 2. A) 5×7 cm, 1-2 mm plaques with erosions and no inflammatory signs were observed on the abdomen's upper right and left quadrants; **B,C**) in the left and right axilla, the skin is dry and scaly, with single papules, that tend to merge into plaques in some places. Abundant excoriations.

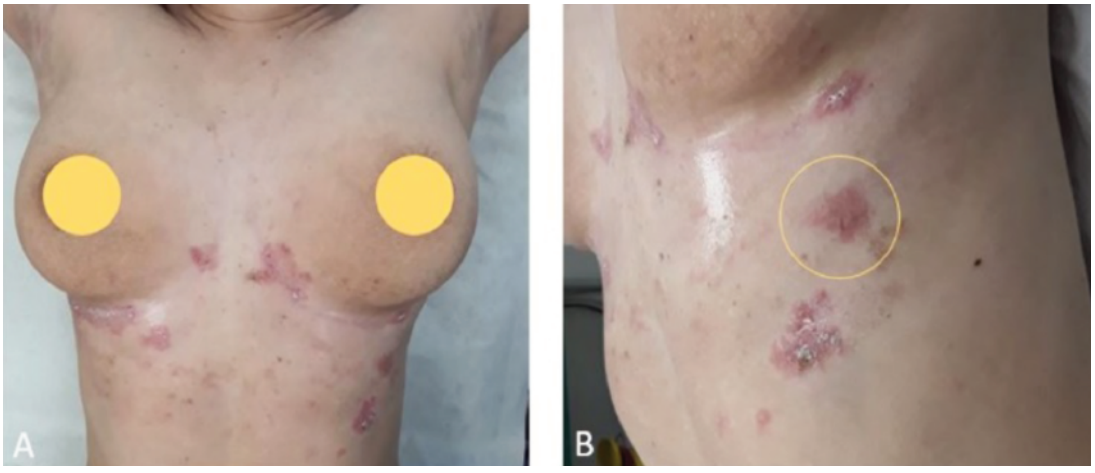

Figure 3. A) Regressing rash in the axilla region, papules that merge to plaques are still visible; **B**) a pink plaque with a diameter of 1.5 cm.

Discussion

Overview of CO_2 laser mechanism, settings, and effects in Hailey-Hailey disease treatment

CO_2 laser ablation has proven to be safe and effective in the most complicated HHD cases, with patients reporting a substantial improvement in their overall quality of life.[5] The best-documented laser therapy for HHD is the continuous CO_2 laser. The mechanism of action of this laser in HHD is thought to involve fibrosis in the papillary dermis, mutant keratinocyte destruction, and regeneration of these cells from the cutaneous adnexa, such as the eccrine glands with normal keratinocytes.[6] The correct choice of laser parameters to achieve the best therapeutic effect is still a highly debated question. One study suggests that an aggressive approach, consisting of 3 passes with a laser output power of at least 25 W, is necessary for CO_2 laser resurfacing to be effective in HHD.[6] In their research, recurrence, or HHD, was more common in cases treated with lower output powers. This leads to the hypothesis that a certain degree of thermal damage is necessary to achieve good results and prevent a recurrence. However, there are cases where a power output of 6 W and 3 passes provided no recurrence of HHD in the treated skin.[7] Larger controlled studies are needed to determine the most satisfactory therapeutic guidelines for CO_2 lasers in HHD. The reviewed literature also notes cases where local recurrence was observed after the first session. If such an incidence occurs, the authors suggest a second CO_2 laser session involving more passes than the first.[6]

Fractional CO_2 laser for Hailey-Hailey disease treatment

The fractional CO_2 laser is, in comparison, an emerging treatment choice for HHD. Its mechanism in HHD is not fully understood. It is hypothesized that partial ablation of the skin with a fractional laser can result in adjacent cells that do not express the mutated gene contributing to epidermal regeneration, thus minimizing healing time, postoperative care, and hospitalization.[8] Four recent case reports described the use of a fractional CO_2 laser for HHD. Laser systems and other parameters varied but overall did not differ substantially from those chosen with continuous CO_2 laser, which we summarized previously. The authors reported marked improvement with no relapses in 3 of the cases and little to no side effects.[9-11] In one case, axillary and submammary lesions healed well, whereas inguinal lesions were refractory.[12] The reviewed literature showcases that treatment with ablative fractional devices could achieve satisfactory results in HHD. Nonetheless, the sparing of involved tissue might lead to disease recurrence in some cases.

Anesthesia during CO_2 laser therapy for Hailey-Hailey disease

In HHD, CO_2 laser resurfacing is primarily limited by pain. The authors agree that topical anesthetics are generally insufficient in larger areas or in areas where more than 2 passes are used.[6] In such cases, local or general anesthesia is indicated. Although some patients prefer to have the procedure performed under general anesthesia, it is found that in many cases, this is not necessary.[13] Moreover, local anesthesia provides safe treatment of large areas with less risk of systemic lidocaine toxicity. In a retrospective study of 13 patients who underwent CO_2 laser ablation for HHD, the use of general anesthesia was chosen when a session had a more aggressive approach (power output of 25-45 W) or treated many anatomic sites.[13] The most common anesthesia tended to be local anesthesia with or without conscious sedation. The authors noted no difference in the therapeutic outcome related to the type of anesthesia used.

CO_2 laser therapy outcomes and side effects in Hailey-Hailey disease

The majority of reported cases document successful treatment of HHD with CO_2 laser abrasion, with no recurrence of lesions at follow-up.[6,9-11,13]

However, it is important to note that some authors report minor recurrence or nearly clear resolution in the treated area.[12,14,15]

The main side effects of CO_2 laser include transient edema, erythema, scarring, and depigmentation.[8] Postoperative pain is moderate to intense in most patients.[13] Recurrence of disease at the periphery of the treated lesion has been documented in some cases, with one study reporting 69.2% of patients with this complication.[13] The application of the laser to an area that extends beyond the clinically visible disease has been theorized as a solution for this phenomenon.[7]

Conclusions

This clinical case supports the idea that CO_2 laser ablation is an effective and safe therapeutic option for HHD and remains the treatment of choice for prolonged remission of recalcitrant plaques with minimal adverse effects. Nonetheless, multicenter clinical studies are necessary to consolidate the long-term efficacy of fractional CO_2 laser for HHD.

References

1. Hailey H, Hailey H. Familial benign chronic pemphigus. Arch Dermatol Syphilol 1939;39:679-85.
2. Chiaravalloti A, Payette M. Hailey-Hailey disease and review of management. J Drugs Dermatol 2014;13:1254-7.
3. Patel VM, Rubins S, Schwartz RA, et al. Hailey-Hailey disease: a diagnostic challenge. Cutis 2019;103:157-9.
4. Farahnik B, Blattner CM, Mortazie MB, et al. Interventional treatments for Hailey-Hailey disease. J Am Acad Dermatol 2017;76:551-8.e3.
5. Ben Lagha I, Ashack K, Khachemoune A. Hailey-Hailey disease: an update review with a focus on treatment data. Am J Clin Dermatol 2020;21:49-68.
6. Pretel-Irazabal M, Lera-Imbuluzqueta JM, Espana-Alonso A. Carbon dioxide laser treatment in Hailey-Hailey disease: a series of 8 patients. Actas Dermosifiliogr 2013;104:325-33.
7. Kruppa A, Korge B, Lasch J, et al. Successful treatment of Hailey-Hailey disease with a scanned carbon dioxide laser. Acta Derm Venereol 2000;80:53-4.
8. Falto-Aizpurua LA, Griffith RD, Yazdani Abyaneh MA, Nouri K. Laser therapy for the treatment of Hailey-Hailey disease: a systematic review with focus on carbon dioxide laser resurfacing. J Eur Acad Dermatol Venereol 2015;29:1045-52.
9. Campuzano-García AE, Torres-Alvarez B, Hernández-Blanco D, Castanedo-Cázares JP. Hailey-Hailey disease improved by fractional CO2 laser. J Cosmet Laser Ther 2015;17:213-5.
10. Grönemeyer LL, Thoms KM, Bertsch HP, et al. Reflectance confocal microscopy and Hailey-Hailey disease: assessment of response to treatment after CO2 laser ablation. J Dtsch

Dermatol Ges 2014;12:1135-7.
11. Da Nobrega Vilela V, Gonçalves da Silva Carvalho C, de Sá Menezes Carvalho G, et al. Treatment of the Hailey-Hailey disease with fractional CO2 laser: a three-case series. Surg Cosmet Dermatol 2017;9:91-3.
12. Ortiz AE, Zachary CB. Laser therapy for Hailey-Hailey disease: review of the literature and a case report. Dermatol Reports 2011;3:e28.
13. Hochwalt PC, Christensen KN, Cantwell SR, et al. Carbon dioxide laser treatment for Hailey-Hailey disease: a retrospective chart review with patient-reported outcomes. Int J Dermatol 2015;54:1309-14.
14. Touma DJ, Krauss M, Feingold DS, Kaminer MS. Benign familial pemphigus (Hailey-Hailey disease). Treatment with the pulsed carbon dioxide laser. Dermatol Surg 1998;24:1411-4.
15. Christian MM, Moy RL. Treatment of Hailey-Hailey disease (or benign familial pemphigus) using short pulsed and short dwell time carbon dioxide lasers. Dermatol Surg 1999;25:661-3.