Laser therapy for Hailey-Hailey disease: review of the literature and a case report

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Abstract

Medical therapy for Hailey-Hailey disease (HHD) generally only provides temporary suppression. Surgical intervention has been shown to prolong remission, but may lead to significant morbidity. Laser therapy is becoming the preferred method of treatment because of its successful results and lower risk of complications compared to surgical modalities. We report a case of fractional ablative carbon dioxide (CO_2) laser treatment for HHD and review the relevant literature. Fractional CO_2 laser therapy was performed in our patient with a 14-year history of HHD. No recurrence was observed 5 months after laser therapy in right inframammary and axillary regions. Symptomatic recurrence was noted after treatment of inguinal areas. In conclusion, traditional laser ablation remains the treatment of choice for prolonged remission of recalcitrant plaques in HHD.

Introduction

Familial benign chronic pemphigus, also known as Hailey-Hailey disease (HHD), is a rare autosomal dominant disease characterized by crusted erosions with marked predilection for intertriginous areas, especially the axillae, submammary and groin regions.[1] The onset of clinical lesions is typically during the second or third decade of life, and may present as late as the fifth decade.[2] The course of the disease is often variable with periods of exacerbation and spontaneous remission. Lesions generally heal without scarring, but may be complicated by malodorous vegetations and painful fissures.

Environmental factors, such as heat, sweating, secondary infections, and allergic contact allergens found in topical treatments, can exacerbate disease severity.[1,3] Friction can also induce new lesions due to defects in cell-cell adhesion within the epidermis. Suprabasilar acantholysis, which causes the characteristic "dilapidated brick wall" appearance, is due to mutations in the Golgi-associated calcium transporter ATP2C1 located on chromosome 3q21-24.[2,4]

First-line therapies for HHD include topical corticosteroids, topical and/or systemic antibiotics, and antifungals. Anecdotal reports have shown some benefit with retinoids,[5] dapsone,[6] cyclosporine,[7] topical vitamin D analogs,[8] and topical immunomodulators[9] in recalcitrant cases. Medical therapies may be beneficial short-term, but generally do not induce prolonged remissions. They are also limited by their long-term use. Therefore, there is a need for more definitive care. Surgical modalities, such as wide excision with split-thickness grafting,[10] primary closure[11] or healing by secondary intention[12] have been reported to achieve prolonged remission and cure in some cases. However, these techniques are cosmetically disfiguring and may be associated with great morbidity such as scar contractures, limited mobility, thromboembolic events, graft failure, or infection.[13,14] More superficial ablative techniques, such as dermabrasion and laser ablation are now favored compared to older more aggressive surgical approaches. Dermabrasion has been reported to achieve extended remission, but is limited to treatment areas that can be immobilized or flattened and is not suitable for genital and mucosal lesions. Several treatments are generally required and hypertrophic scarring has been reported.[15]

Laser therapy of HHD is a more advanced technique that can be used in sites where dermabrasion is not feasible. Traditional ablative lasers such as carbon dioxide lasers and erbium:YAG laser devices have been well documented as options for treatment of recalcitrant plaques in HHD. To our knowledge, we are the first to report a case of HHD treated with a fractionated ablative laser. Fractionated ablative lasers are becoming more commonly used for resurfacing procedures due to their excellent results, better safety profile, and decrease in downtime compared to traditional ablative devices. However, in the authors' opinion, fractionated ablative devices are not particularly effective for treatment of HHD.

Carbon dioxide lasers

The most well documented laser therapy in the treatment of HHD is the carbon dioxide laser (CO_2) (Table 1). Don *et al.*[16] reported the first case of HHD successfully treated with CO_2 laser abrasion. The patient was a 50-year-old male who had failed conventional therapeutic regimens. After CO_2 laser treatment, the patient remained free of disease in treated areas 8 months after therapy. Although, the patient was kept on oral prednisone and oral antibiotics during laser therapy, only untreated areas flared. The authors suggested that the sparing of underlying adnexae contributed to the reepithelialization of normal epidermis.[16] This report led to several other cases of localized, recalcitrant plaques in patients with HHD that have been successfully treated with CO_2 laser vaporization.

Kartamaa *et al.*[17] reported the largest case series of 8 patients with HHD treated with CO_2 laser vaporization (Sharplan 1020, Laser Industries Ltd., Tel Aviv, Israel). Six of the 8 patients had symmetrical skin lesions of which one side was left untreated for an internal control. Five of these 6 patients showed considerable improvement in the treated side compared to control. Notably, 2 of the patients also had spontaneous resolution in untreated lesions. Of the 2 patients without internal controls, both patients showed improvement. At follow-up visits ranging from 10 to 27 months, only 2 of the patients had recurrent lesions in the treated sites. Hypertrophic scarring was noted in the axillary region of 1 patient. The authors speculated that improvement in skin lesions was secondary to fibrosis of upper dermal tissues which led to increased support of diseased epidermis.

Touma *et al.*[18] reported a case of a 38-year-old woman with HHD treated with a pulsed CO_2 laser (UltraPulse 5000, Coherent Medical Group, Palo Alto, CA, USA) to unresponsive lesions of the chest and axilla. These areas showed clearing in 1 to 2 weeks. They also investigated the effects of treating uninvolved skin for prophylaxis. The uninvolved area only had a minor asymptomatic recurrence 18 months after treatment. Minor scarring was noted on the chest.

Christian *et al.*[19] treated a 26-year-old woman with refractory HHD of the axillary regions with a short dwell time CO_2 laser. She received additional treatments with a short pulsed CO_2 laser to foci of persistent blistering. This resulted in prolonged resolution of disease in the right axilla and periodic blistering in the left axilla at 3 years following laser therapy. The authors later mention that because the right axilla was initially treated with a con-

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tinuous CO_2 laser and the left axilla was treated with fewer passes and a lower fluence, the thermal damage may have been insufficient to provide adequate disease control. Therefore, the authors proposed that short pulsed CO_2 lasers may not be as effective as continuous CO2 lasers in treating HHD due to their lower fluences.

McElroy *et al.*[20] reported a 56-year-old female with HHD treated with a CO_2 laser (Weck 525, Weck Instruments, Princeton, NJ, USA) to the inguinal and perivaginal areas and a 38-year-old male treated similarly on the scrotum. Both patients remained disease free at 4 months and 1 year, respectively, following treatment.

Kruppa *et al.*[21] reported 2 patients with HHD that were successfully treated with a CO_2 laser (SilkTouch Flashscanner, Laser Industries Ltd., Tel Aviv, Israel). They did not report any complications and remained without recurrence in treated skin at 6 months and 1 year following laser therapy. The authors suggested that perhaps the flash scanner may decrease the risk of scarring due to rapid energy delivery. This report reaffirmed that CO^2 laser ablation is an effective treatment modality for HHD.

Erbium: YAG Lasers

Beier *et al.*[22] reported the first cases of HHD treated with an erbium:YAG 2940-nm laser (MCL 29 Dermablate, Asclepion-Meditec, Jena, Germany) (Table 1). Two male patients with HHD were treated for malodorous lesions of the groin, scrotum, and axillae. One of the patients showed complete regression in treated areas 1 year following laser therapy. The other patient had recurrence of a lesion at the periphery of the treated area, which required an additional treatment. There were no reported side effects in these patients. The authors concluded that erbium: YAG laser ablation is very effective in treating HHD and perhaps superior to CO_2 laser ablation because it produces less residual thermal injury and therefore, has a lower risk of scar formation.[23] They also hypothesized that the key to improvement is related to the critical depth of tissue removal.

Konrad *et al.*[24] compared erbium:YAG laser ablation (MCL 29 Dermablate, Asclepion-Meditec, Jena, Germany) to dermabrasion and botulinum toxin A (BTXA) injections (Botox, Allergan, Irvine, CA, USA) in the treatment of a 62-year-old woman with HHD. Since it is well known that sweating can exacerbate disease,[1] this patient was treated with 100 IU of BTXA to the submammary regions to control hyperhidrosis. After cessation of sweating, the patient was treated with dermabrasion on one side and a pulsed erbium: YAG laser on the other. Designated areas were left unablated to assess the efficacy of BTXA alone. All treated areas were free of disease 12 months after treatment. However, the patient reported an

Table 1. Laser therapy for Hailey-Hailey disease.

Author	Laser Used/Parameters	n.	Results
CO_2 Lasers			
Don *et al.*[16]	CO_2 laser (Power of 8 W, irradiance of 1020 W/cm2, 1-mm spot, defocused mode, continuous wave)	1	No recurrence in treated areas at 8 months after treatment.
Kartamaa *et al.*[17]	Sharplan 1020, Laser Industries Ltd. (Power of 5 W, irradiance ranging160 - 635 W/cm^2, 1-2 mm spot, continuous wave)	8	At follow-up visit (10-27 months), no recurrence of lesions in 5 of 8 patients
Touma *et al.*[18]	UltraPulse 5000, Coherent Medical Group (Settings not provided)	1	Treated lesional skin showed clearing in 1-2 weeks. At 18 months following therapy, prophylactically treated skin had a minor asymptomatic recurrence. Minimal scarring was reported.
Christian *et al.*[19]	Short dwell time CO_2 laser (396 μsec dwell time, energy of 25-28 J/cm^2, 2-3 passes) Short pulsed CO_2 laser (90 μsec pulse duration, energy of 15 J/cm^2) Continuous CO_2 laser (396 μsec pulse duration, energy of 28 J/cm^2, 3 passes)	1	Nearly complete resolution of lesions treated with continuous CO_2 laser and short dwell time CO_2 laser 3 years after treatment. Periodic blistering in lesions treated with short dwell time CO_2 laser only.
McElroy *et al.*[20]	Weck 525, Weck Instruments (Power of 5-15 W, 2.0 mm spot, defocused mode, 2 passes)	2	Lesions treated remained without recurrence at 4 months and 1 year.
Kruppa *et al.*[21]	SilkTouch Flashscanner, Laser Industries Ltd. (Power of 6 W, 3 mm spot, 0.2 sec scan time, 3 passes)	2	Patients remained without recurrence in treated skin at 6 months and 1 year.
Erbium:YAG Lasers			
Beier *et al.*[22]	MCL 29 Dermablate, Asclepion-Meditec (1.6-5.0 mm spot, 5-10 Hz, 300-1000 mg, energy of 5-8.5 J/cm^2, and 350 microseconds, 30% overlap)	2	One patient showed no recurrence and the other patient had recurrence at the periphery of treated lesions 1 year after therapy.
Konrad *et al.*[24]	MCL 29 Dermablate, Asclepion-Meditec, (3 mm spot, 450 mJ, 8 Hz,) dermabrasion, and Botox, Allergan 100 IU	1	Sites treated with dermabrasion, laser ablation and BTXA alone remained relapse free for 12 months. Increased healing time with laser treatment compared to dermabrasion. BTXA was as effective as ablation.
Radiofrequency Ablation			
Nandini *et al.*[25]	Surgitron FFPF EMC, Ellman International, Inc. (3.8 MHz, 140 Watt +/- 20%, continuous mode)	1	Treated lesions remained clear 16 weeks after therapy.
Vascular Lasers			
Fisher *et al.*[26]	V-beam, Candela Corporation (595 nm, 10-mm spot, 1.5 ms, and energy of 7.5 J/cm^2)	1	The patient had continuous remission over 20 months.
Diode Lasers			
Downs[27]	Smoothbeam, Candela Corporation (6 mm spot, energy of 14 J/cm^2, DCD 50 ms)	1	After 3 treatments, no improvement in lesions. Marked reduction in sweating and malodour.

extended healing time in the laser treated area compared to the area treated with dermabrasion. In this case, the authors reported that BTXA alone was as effective as ablation.

Radiofrequency ablation

Although, radiofrequency is not considered a laser, it is included in this review for interest due to its ability to cause tissue ablation (Table 1). Nandini *et al.*[25] reported a case of a 35-year-old male with HHD with a 20-year history of recurrent axillary erosions that were successfully treated with radiofrequency ablation (Surgitron FFPF EMC, Ellman International, Inc., New York, NY, USA). The authors ablated one axilla to the level of mid-dermis with clearance of the lesions 16 weeks after therapy. The opposite side was left untreated as the internal control and was reported to have flared several times compared to the ablated side. Radiofrequency was determined to be a cheap, effective and easily administered treatment for HHD.

Vascular lasers

Fisher *et al.*[26] treated a 35-year-old female with persistent HHD for steroid induced striae-rubrae of the entire axillary and inframammary regions with a pulsed-dye laser (PDL) (V-beam, Candela Corporation, Wayland, MA, USA) (Table 1). After the fourth treatment, the patient reported incidental improvement in the axillary and inframammary regions, while she continued to flare in the untreated inguinal area. The patient continued to have remission of her disease over the next 20 months with additional PDL treatments at purpuragenic settings approximately 1 month apart. The rationale they offered for improvement was in relation to a vascular effect or some unknown effect of PDL on keratinocytes. The authors did not investigate the efficacy of nonpurpuragenic settings, but suggest PDL as a potential treatment in all skin types with a good safety profile.

Diode lasers

Downs[27] reported the only case of HHD treated with a 1450-nm diode laser (Smoothbeam, Candela Corporation, Wayland, MA, USA) (Table 1). The author reported no improvement in the lesions regardless of a marked reduction in sweating. The mechanism of decreased sweat production was not explored. The author concluded that subsurfacing laser treatment is not an effective treatment for HHD.

Fractional ablative lasers: case report

A 49-year-old female presented to our clinic with a 14 year history of HHD with recalcitrant, symptomatic, hyperkeratotic, fissured plaques in the axillary, inframammary and groin areas. Her father was similarly affected. She failed conservative medical therapy with topical and oral antibiotics, topical antifungals and topical corticosteroids. She had good improvement with oral corticosteroids, but did not want to be on long-term therapy due to their potential side effects. She also responded well to dapsone, but was discontinued secondary to an adverse reaction. The patient continued to flare with strenuous exercise and was interested in a more definitive treatment, but did not want to undergo radical surgery.

Given that there is a better safety profile and less downtime associated with fractional ablative laser therapy compared to traditional ablative devices, we decided to treat our patient with a fractionated ablative CO_2 laser (Fraxel re:pair, Solta Medical, Inc., Hayward, CA, USA). A 4x2 cm test site on the left submammary region was treated with 4 passes at a fluence of 70 mJ and 30% coverage. Two months after therapy, the test site was much improved clinically and symptomatically. She then underwent treatment to her right axillary, inframammary and inguinal regions in the same manner using tumescent anesthesia. The patient received antiviral prophylaxis and standard postoperative care with vinegar soaks and petroleum jelly applications. The opposite side was left untreated as an internal control. The patient was kept on topical steroids and topical antibiotics during the course of laser therapy in order to maintain control of the untreated sites.

One month following treatment, the right axilla (Figure 1) and right groin were improved, but the right submammary region was slow to heal and still mildly tender with residual ulceration. Overall, the patient was very happy with the results and requested additional therapy for the eroded, grey, hyperkeratotic plaques on the left groin. The left groin region was treated with similar settings, but did not respond as well as previously treated areas. The patient returned to the clinic several months later with persistent painful, erosive, hyperkeratotic plaques on bilateral inguinal folds. Given the failed response to fractionated CO_2 laser therapy, the patient was treated with a traditional erbium:YAG 2940-nm laser (Profile, Sciton, Inc., Palo Alto, CA, USA) with 2 passes at an ablation depth of 50 μm and a coagulation of 25. She returned one month later with tremendous symptomatic improvement and only residual erosions and hyperkeratosis.

Discussion

HHD is a frustrating disease with chronic recalcitrant erosive plaques that can be very debilitating. Although, first line therapy is generally medical, these options only provide temporary suppression. Surgical options can lead to prolonged remissions, but are not without complications. The more recent trend in therapy has been in using superficial ablative techniques. Dermabrasion has been effective, but is limited by the treatment sites and risk of complications. This has led to laser therapy as the preferred modality for treating recalcitrant plaques in HHD. However, our experience is limited to anecdotal reports.

The exact mechanism of action of laser ablation for the treatment of HHD remains unclear. One theory is that the epidermis and keratinocytes that express the molecular defect are ablated, while leaving adnexae intact to regenerate normal epidermis lacking the adhesion defect. Another theory is that dermal fibrosis leads to better support of the diseased epidermis and decreases risk of ulceration and fissuring. This hypothesis supports the improvement seen in non-ablative laser therapy.

Fractionated technology only ablates microthermal zones and therefore, leaves untreated areas of epidermis expressing the

Figure 1 A) Right axilla prior to laser treatment. B) Right axilla 1 month after treatment with fractional CO_2 laser therapy.

molecular defect. Perhaps with several treatments, eventually the entire diseased epidermis would be completely ablated and would lead to some improvement. However, this is only speculation. At this time, the authors do not recommend fractional ablative lasers in the treatment of HHD since traditional ablative devices seem to provide more consistent results than seen in our patient. Further studies are needed to determine optimal devices and laser parameters for treatment of HHD.

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