

Treatment of Epidermal Hamartomas: Review and Description of Treatment With Electrodesiccation and Combination Laser Therapy

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Congenital epidermal nevi encompass inflammatory linear verrucous epidermal nevus (ILVEN), epidermal nevus, and nevus sebaceous. These hamartomas have been treated with several different modalities and can pose a therapeutic challenge depending on the location, size, nature, and thickness of the lesion. We review the treatment options for these lesions, which include topical therapies, systemic therapies, destructive therapies, and laser therapies. We also describe the successful use of electrodesiccation and the combined Erbium:YAG and CO₂ lasers to treat these skin conditions. We suggest personalizing therapy for each patient depending on the area of involvement, the size of the lesions, the nature of the lesions (keratotic vs fleshy), and the thickness of the lesions.

Inflammatory linear verrucous epidermal nevus (ILVEN) is a benign cutaneous hamartoma characterized by erythematous, pruritic, inflammatory papules that occur as linear bands along the lines of Blaschko. The cause and pathogenesis of ILVEN are unclear. Studies have reported clinical and histologic similarities between ILVEN and psoriasis.¹ There is direct

and indirect evidence that IL-1, IL-6, tumor necrosis factor- α , and intercellular adhesion molecule-1 are up-regulated in ILVEN, similar to psoriasis.¹ However, there was a reduction in the number of Ki-67–positive nuclei and an elevation in the number of keratin 10–positive cells and HLA-DR expression in ILVEN compared to psoriasis.² Combining both observations, elevated intercellular adhesion molecule-1, endothelial leukocyte adhesion molecule-1 and HLA-DR expression in ILVEN suggests an inability to down-regulate the inflammatory infiltrate.¹ Epidermal nevi are hamartomatous lesions resulting from excess keratinocyte production that typically present at birth and whose types include verrucous epidermal nevus, ichthyosis hystrix, systematized nevus, and nevus unius lateris. These nevi can be found alone or in association with epidermal nevus syndrome, which can have neurologic, ocular, skeletal, and cardiovascular manifestations.

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Nevus sebaceous is a congenital hamartoma where malformed sebaceous glands predominate. The lesion appears as a yellow-orange, waxy papule or plaque seen most commonly on the head and neck. Although these conditions are benign, patients seek medical treatment for relief of discomfort and for cosmetic concerns.

Numerous treatment modalities have been utilized to treat ILVEN, epidermal nevi, and nevus sebaceous. These therapies range from topical to systemic to destructive to laser. We review these multiple options in order to provide a clear understanding of how to approach these challenging patients. The ultimate objective is to offer patients the most amount of cosmetic improvement with the least amount of morbidity. In general, topical and systemic therapies have variable results, surgical excision is limited when treating extensive disease, and aggressive laser therapy on nonfacial skin is fraught with the risk of scarring.

TOPICAL THERAPIES

Topical therapies are noninvasive methods of treating these lesions. Numerous types of topical agents have been described to alleviate symptoms, such as pruritus, and to resolve the lesions. One of the oldest reported topical therapies to treat ILVEN, dithranol, was found to result in complete relief from itching and clearance of all linear lesions except for a small verrucous band on the shin.³ Dithranol blocks DNA replication, thus slowing the excessive cell division. The immediate response to dithranol is best explained by the assumption that many of the lesions in this case of ILVEN represented true linear psoriasis.³ However, long-term follow-up was not performed. Topical corticosteroids have been reported to improve the symptoms of these inflammatory lesions. One study found that pruritus as well as inflammation slightly improved with application of a topical corticosteroid and petrolatum ointment containing salicylic acid but did not produce complete resolution.⁴ Mutasim⁵ used the combination of tacrolimus ointment 0.1% and fluocinonide ointment 0.05% in one patient to successfully treat ILVEN that extended from the right foot to the right buttock.

Böhm et al,⁶ however, reported a patient with a 2-year history of ILVEN located on the upper right arm that was treated with corticosteroids, antibiotics, and antimycotics with little or no improvement. This patient was then treated with calcipotriol ointment 0.005% to near complete resolution after 8 weeks and no relapse 25 weeks after withdrawal.⁶ Another study found that calcipotriol ointment had the advantage of having no substantial irritation potential and did not have the risk of contact sensitization, phototoxicity, or photosensitization.⁷ Zvulunov et al⁸

also reported the success of calcipotriol ointment in the treatment of 2 patients with ILVEN with the most prominent effect of this medication in these patients to be the rapid relief of pruritus. Garg et al⁹ noted that cost of this medication is a limiting factor. Furthermore, regular or intermittent treatment with calcipotriol ointment only brings the patient under temporary remission.⁹ These studies suggest that calcipotriol can achieve complete resolution and can alleviate pruritus; however, this is a costly medication that provides temporary relief, resulting in flares when this medication is discontinued. A limitation of these studies is that sample sizes are one to 2 patients. Overall, the studies above suggest that topical therapy provides temporary, symptomatic relief but does not provide a permanent solution.

Another topical therapy, a 1:1 combination of tretinoin cream 0.1% and 5-fluorouracil cream 5% under semi-occlusion, was used for 2 months with excellent response to treat a patient with linear verrucous epidermal nevus on the right side of the face that extended from the forehead to the base of the neck.¹⁰ This treatment was well tolerated but discontinuation resulted in recurrence.¹⁰

Chemical peels are another topical therapy that has been reported to treat ILVEN. Toyozawa et al¹¹ reported a patient with ILVEN whose lesions responded effectively to trichloroacetic acid (TCA) peeling treatment.¹¹ Specifically, TCA peels 60% were applied on whole lesions of ILVEN on the lower leg 40 times with an average TCA application time of 2 minutes. The eruptions improved gradually and these good conditions have been maintained for more than 2 years. However, this treatment did not produce complete resolution. The advantages of this technique are that it is simple to perform, there is minimal pain, and there have been no generalized side effects.¹¹ The downfall of this method are the numerous treatments required to obtain improvement and that the high dose of TCA used can cause notable scarring if it gets onto unaffected skin.

SYSTEMIC THERAPIES

Few oral medications have been implemented in the treatment of these lesions, including biologic and retinoid therapies. Bogle et al¹² described a patient with widespread ILVEN on the face, trunk, and all extremities who improved with etanercept. Etanercept was initially considered to treat this patient because of the clinical and histologic similarities between ILVEN and psoriasis. This study suggests that etanercept and other biologic therapies used in the treatment of psoriasis should be considered in the treatment of widespread ILVEN.¹²

Renner et al¹³ reported a patient with ILVEN who was successfully treated with acitretin. Of note, this treatment

initially increased the inflammatory component of ILVEN, requiring intermittent reduction of dosage. Otherwise, side effects were minimal with dryness of the lips only.¹³

A combination of systemic therapies plus phototherapy also has been applied to treat ILVEN. Ozdemir et al¹⁴ described a patient with widespread plaque-type psoriasis and localized ILVEN on the extensor surface of the right hand and forearm who was treated with low-dose acitretin for the first week, then narrowband (TL-01) UVB phototherapy in the second week that was then applied 3 times weekly with whole-body exposure units for 8 weeks. The treatment was well tolerated and a good response was obtained in the psoriasis and ILVEN lesions. However, relapse occurred in psoriasis and ILVEN lesions after 10 months and etanercept treatment was initiated. Etanercept helped the psoriatic lesions but not the ILVEN lesions. This acitretin narrowband TL-01 UVB phototherapy appeared to be very effective in the treatment of the localized ILVEN, reducing the inflammatory components and pruritus.¹⁴ This study also commented on the histologic similarities between ILVEN and psoriasis but reported the ineffectiveness of etanercept in treating ILVEN, which is a sharp contrast from the study by Bogle described above.¹²

DESTRUCTIVE THERAPIES

This section includes destructive modalities such as cryosurgery, electrodesiccation with or without curettage, and surgical excision.

Fox and Lapins¹⁵ reported the success of cryotherapy using liquid nitrogen in a patient with ILVEN. Although cryotherapy does not provide an easy or dramatic cure, the authors believe that it does produce reasonably good cosmetic results.¹⁵ Another study described the efficacy and safety of cryosurgery for the treatment of epidermal nevi. Nine patients with verrucous epidermal nevi and 2 patients with extensive unilateral epidermal nevus were treated with cryosurgery consisting of 2 cycles of open spray technique, 10 to 15 seconds each.¹⁶ Cosmetic result was excellent with no scarring. However, 1 patient showed a relapse within 8 months after treatment and 1 patient initially developed hypochromic scarring but had repigmentation after 6 months. These authors present cryosurgery as a low cost, simple technique with a good cosmetic result.¹⁶

We have used electrodesiccation with and without curettage successfully to address epidermal nevus and nevus sebaceous. This modality is simple, well-tolerated, produces a good cosmetic result, and is cost-effective as the machine is very inexpensive. The senior author uses the Hyfrecator 2000 (ConMed Corporation) on a low (unit comes with low and high settings) setting of 1.8

to 3.4 W. The choice to use electrodesiccation is based on the characteristics and location of the lesion. "Fleshy" (epidermal nevus) or "soft" (nevus sebaceous) well-circumscribed lesions on the face are most amenable to this modality with the least morbidity. This modality is also used to reduce the hyperkeratotic areas of ILVEN to make the ILVEN lesion more amenable to laser ablation. This modality can be combined with shave excisions of very elevated portions of the lesion followed by electrodesiccation of the remaining portion on the same day.

Typically the hyperkeratotic (ILVEN) or raised "fleshy" (epidermal nevus) portions of the lesion are treated with electrodesiccation on a low setting, using a spatula tip to simply desiccate the raised portion while leaving the normal adjacent skin untouched. If the lesion is very verrucous after the electrodesiccation, a curette is used to gently remove the treated areas, and the remaining lesion is electrodesiccated again, keeping the power setting low. Treatments can be repeated safely at 6-week intervals until the desired result is achieved. Between treatments, patients are instructed to use topical tazarotene cream 0.1% or tretinoin cream 0.1% to keep regrowth to a minimum.

Nevus sebaceous lesions are treated with electrodesiccation on a low setting. However, an epilating needle is utilized to pierce the skin thus allowing the physician to treat the portions of this lesion, which are deep in the surface of the skin. Care is taken not to pulse for more than 1 second in any given area so as to avoid creating "ice pick" scarring or sinus tracts. Usually, curettage of these lesions is unnecessary. Once healed, these lesions are treated with topical tazarotene or tretinoin as well.

Surgical excision has been performed with different methods to treat ILVEN, epidermal nevi, and nevus sebaceous. Bazex et al¹⁷ described the treatment of verrucous epidermal nevus with razor blade shaving using a dermatome, followed by phenol-peeling on the pigmented areas of the face, which produced a good cosmetic outcome. Dellon et al¹⁸ described partial-thickness skin excision to treat epidermal nevi. The patient treated showed disease-free areas but healed with hypertrophic and keloid scars.¹⁸ Lee et al¹⁹ reported 4 patients with extensive ILVEN treated successfully with full-thickness surgical excision. These authors recognize that surgical modalities carry the risk of marked scarring and a high rate of recurrence.¹⁹ These studies describe numerous surgical methods but recognize the adverse effects of scarring and recurrence and the limitation of performing such an invasive procedure in lesions that span the entire body.

LASER THERAPIES

A variety of lasers have been described to treat ILVEN, epidermal nevi, and nevus sebaceous.

Photodynamic Therapy

Parera et al²⁰ described a patient with ILVEN who showed an excellent and long-standing response to photodynamic therapy (PDT) using red light (570–670 nm) with methyl aminolevulinate (MAL). In et al²¹ reported 12 patients that were treated with topical 5-aminolevulinic acid (ALA) 20% or MAL after carbon dioxide (CO₂) laser ablation at 1- to 4-week intervals. The lesions were irradiated with light emitting diode device and clinical improvement was visually assessed at one month after treatment. The majority (7/12) of the patients showed moderate improvement, which was defined as 51% to 75% decrease in lesional volume. Two patients showed marked improvement, more than 75% decrease of lesional volume.²¹ There were no considerable side effects.²¹

Kim et al²² reported a case of a patient with facial nevus sebaceous that was treated with variations of PDT. Initially the lesion was treated by applying ALA cream 20% and exposing it to intense pulsed light. In subsequent sessions, the lesion was first ablated with either CO₂ laser or erbium:YAG (Er:YAG) laser prior to PDT with intense pulsed light. Later, the lesion was treated with Er:YAG fractional laser and then MAL 160 mg/g cream with red light irradiation. The study found that ablative PDT and fractional PDT had results that were superior to simple PDT, but the effects were primarily transient. There was a definitive but transient decrease in sebum production and destruction of the sebaceous glands. Overall, the authors were not able to achieve long-lasting clinical improvement after PDT.²²

Pulsed Dye Laser

Alster²³ describes the successful treatment of ILVEN with 585-nm flashlamp-pumped pulsed dye laser in which authors noted decreased pruritus as well as partial resolution of the lesion in one patient, with stable results at 1-year follow-up.

Ablative Lasers

The use of ablative lasers captures the laser wavelength's affinity for water to vaporize tissue in a controlled manner. The literature, as discussed below, described the use of 2 different laser wavelengths for tissue ablation in these disorders: Er:YAG and CO₂. Typically, longer wavelengths penetrate more deeply into the skin. The exceptions to this rule are the ablative wavelengths including CO₂ and Er:YAG. Er:YAG lasers (2940 nm) and CO₂ lasers (10,600 nm) have tremendous affinity for water which results in ablation of the targeted tissue and limits the depth of penetration of the laser beam. The Er:YAG laser has the highest affinity for water, followed by the CO₂ laser.

Er:YAG Laser

Pearson and Harland²⁴ reported using pulsed Er:YAG laser to treat 6 patients with epidermal nevi. Specifically, a pulsed 2940-nm Er:YAG laser at 0.4 to 0.45 J/cm² with 2-mm spot size at 4 pulses was used with excellent cosmetic results at follow-up from 6 to 60 months. The authors attribute favorable results on the selection of cases with superficial or small, discrete lesions, which could be ablated accurately. This study presents pulsed Er:YAG laser as an effective treatment for relatively nonverrucous or papular epidermal nevi.²⁴

Park et al²⁵ assessed the long-term results of Er:YAG laser in 20 patients with verrucous epidermal nevi. Twelve patients were treated with variable-pulsed Er:YAG laser, a 5-mm handpiece at the setting of 7.0 to 7.5 J/cm², at 500-ms pulse duration; 8 patients were treated with dual-mode Er:YAG with a 2-mm handpiece at the setting of 6.3 J/cm², at 350-ms pulse duration (25µm ablation). Fifteen patients showed clearance of their nevi after a single laser treatment and 5 patients showed a relapse within 1 year after the treatment. Notably, no scarring was observed.²⁵

CO₂ Laser

Numerous studies report the efficacy of CO₂ laser treatment. Reports date back to the 1980s. Ratz et al²⁶ presented CO₂ laser vaporization of epidermal nevi in 15 patients over a 5-year period and proposed this technique as an alternative and effective surgical method for the successful removal of these lesions. In the 1990s, Hohenleutner and Landthaler²⁷ compared the treatment of verrucous epidermal nevi in 43 patients with either argon laser coagulation or with CO₂ laser vaporization. The argon laser was effective in treating soft, papillomatous lesions but was ineffective in hard, keratotic nevi. The CO₂ laser was effective in the hard, keratotic nevi but with a tendency to form hypertrophic scars.²⁷ Molin and Sarhammar²⁸ reported a case of disfiguring ILVEN of the vulvar area that was successfully treated with low fluence CO₂ laser. The patient remained improved 2 years following laser therapy.²⁸ Thual et al²⁹ evaluated the efficacy of continuous CO₂ laser therapy in the treatment of verrucous epidermal nevus. This was a retrospective study concerning 21 patients treated for epidermal nevus by CO₂ laser that showed that continuous-wave CO₂ laser is an easy and effective treatment of verrucous epidermal nevus. The authors concluded that aesthetic results are satisfying but moderate recurrences often occur (38% of patients).²⁹

Numerous studies also have investigated pulsed CO₂ laser therapy. Michel et al³⁰ describes 5 patients with

ILVEN and 5 patients with linear verrucous epidermal nevus both treated with superpulsed CO₂ laser. Treatment was effective in all but 2 cases. Slight hyperpigmentation, transitory desquamation, and erythematous papules were observed, and there was no recurrence at 2 years follow-up.³⁰ Boyce and Alster³¹ outlined the successful use of a short-pulsed CO₂ laser in the long-term eradication of epidermal nevi in 3 patients. A pulsed CO₂ laser was used to vaporize the lesions using a 500-mJ pulse energy, 3-mm spot size, and 7 W of power. Effective intra-operative hemostasis was achieved with excellent lesional visualization. No lesional recurrence was observed 10 to 13 months after treatment except in one small area on the ankle in 1 patient.³¹

Paradela et al³² described 25 patients with verrucous epidermal nevi who were treated with CO₂ laser in the superpulsed mode, focalized at 2 W/cm². With a follow-up period of 4 to 79 months, good results were achieved in 92% of patients with soft, flattened nevi and only 33% of patients with keratotic nevi. The authors concluded that CO₂ laser in superpulsed mode is an effective and safe treatment for verrucous epidermal nevi and provides fewer recurrences than other laser therapies. Furthermore, this study postulates that the greatest determining factor for the cosmetic result is the thickness of the nevus.³²

The pulsed CO₂ laser has several advantages over continuous-wave devices.³³ Target lesions can be flattened with precise control of depth of ablation. Each laser pass vaporizes a limited amount of tissue, and a series of such thin slices can be removed to reach the desired end point. In contrast, Er:YAG lasers provide similar precision in tissue removal, but there exists difficulty in achieving hemostasis.³³ Another benefit of CO₂ laser is that it imparts high energy to a small area, thus allowing exact ablation of lesions with minimal damage to surrounding normal tissue.³⁴

Er:YAG + CO₂ Laser

Newer, modified Er:YAG systems have been developed as attempts to approximate the results seen with CO₂ lasers. Some of the newer Er:YAG lasers, allow the use of longer pulse widths (up to 500 μ s) to produce a larger zone of thermal necrosis, which comes closer to mimicking that seen with CO₂ lasers. This results in deeper tissue penetration and improved coagulation of dermal vessels. Another Er:YAG laser system is a "blend" of both CO₂ and Er:YAG (Derma-K, ESQ Medical) lasers that can deliver a pulse of energy composed of both Er:YAG and CO₂. The percentage of CO₂ in each laser pulse can be adjusted from 0% to 100%. This system also offers more coagulation and tissue-tightening than traditional

Er:YAG systems with a side-effect profile more favorable than that of straight CO₂ laser resurfacing.

We describe cases in which we used the combined Er:YAG and CO₂ laser to provide the ablation of Er:YAG and the hemostasis of CO₂. Erbium:YAG lasers have a 25-fold affinity for water as compared to CO₂ lasers. This makes Er:YAG lasers very effective tissue-vaporizers, thus accounting for their ability to ablate tissue thoroughly. However, it is this same characteristics that makes Er:YAG lasers ineffective for hemostasis. The Er:YAG laser vaporizes tissue while leaving minimal residual tissue damage in the surrounding tissue. On the other hand, CO₂ lasers leave behind a zone of tissue necrosis and a zone of tissue thermal damage; this results in the desired hemostatic effect. The combination of both lasers allows the physician to utilize the potential of each laser for the modality it is best used for.

CASE REPORTS

Patient 1

A 17-year-old female with an epidermal nevus extending in a dermatomal fashion along the right angle of the mandible (Figure 1A) presented. Given the risk of hypertrophic scarring with surgery along the mandible, it was felt that conservative therapy was the best option, especially in such a young patient. The raised areas of this lesion were shaved flat followed by electrodesiccation (with a spatula tip) and gentle curettage of the area. She underwent a subsequent treatment one year later with electrodesiccation (Figure 1B). She was continued on maintenance tazarotene cream 0.1% and is shown at 1 year following her last treatment with good improvement and no scarring (Figure 1C).

Patient 2

A 41-year-old woman presented with ILVEN extending along the entire length of the left posterior leg (Figure 2). The patient is mainly bothered by the hyperkeratotic portions of the ILVEN which cause pain and bleeding, and furthermore, by the cosmetic appearance of the area.

Laser resurfacing had been done on a small area of her calf with an unknown type of laser several years prior to coming to the office. She had improvement in the lesion in that area with minor hypopigmentation and no substantial recurrence but with new lesions at the periphery of the treated area.

The patient was started on a topical regimen in order to minimize the thickness of the lesion. She had improved slightly with topical lactic acid cream 12% in the morning and tazarotene cream 0.1% every evening for 6 months. However, the patient desired more significant



Figure 1. Patient at baseline showing fleshy, verruciform, coalescing papules along the right mandibular region in a dermatomal pattern (A). One year after shaving the most raised portion of the lesion along with electrodesiccation of the remaining lesion. This photo is taken prior to a second session of electrodesiccation alone (B). One year following both sessions with good resolution and maintenance using topical tazarotene cream 0.1% only (C).

improvement and was scheduled for laser resurfacing. She understood the risk of permanent hypopigmentation and scarring but felt that she could hide that better than a raised lesion that snags on certain pants and stockings.

The patient underwent tumescent anesthesia of the area to be treated with lidocaine solution 0.2% with epinephrine in a 1:500,000 concentration. This was injected with a 20-mL syringe connected to a 20-gauge spinal needle. Once adequate anesthesia was achieved, laser ablation of the area was carried out with the Er:YAG + CO₂ laser. The laser was set in dual mode at 1.7 J Er:YAG, 4-mm spot size, 35% CO₂, 5 W, and a 10% overlap with a scanner. We chose 35% to allow for some CO₂ laser ablation but not enough to increase the risk of scarring and hypopigmentation. Two passes were performed over the affected area and over a 2- to 3-mm margin of normal tissue to target any subclinical clonal cells as well. The laser was then set in dual mode at 1.7 J Er:YAG, 2-mm spot size, 35% CO₂, 5 W, and 4 to 6 pulses over the remaining hyperkeratotic areas until normal dermis was evident and the lesion was flush with the surrounding skin. Additionally, one area of severe hyperkeratosis (near the Achilles tendon) was first shaved flush to unaffected skin and then treated as above.

The patient was started on oral cephalexin 500 mg twice a day for 2 weeks starting the day before surgery. She was instructed to wash the area 2 to 3 times a day and to apply a bland, petrolatum-based ointment

to the area. She healed uneventfully. At her 10-week postoperative visit, she had residual erythema, which has been fading. She was happy that the pain she had with wearing shoes that hit her Achilles tendon was gone. However, she was noted to have a slight recurrence at 1 area (Figure 3A). The remaining areas have continued to heal well (Figure 3B). At this point, the patient was instructed to resume tazarotene cream 0.1% and lactic acid cream 12%.

As discussed above, a variety of lasers have been utilized to treat ILVEN. This case illustrates the use of 2 distinct lasers in dual mode to target different components of ILVEN. Because Er:YAG lasers have a higher affinity for water than CO₂ lasers, they are potent tissue-vaporizers, enabling our patient's inflammatory areas to be ablated thoroughly. CO₂ laser also provides high energy to a small area allowing exact ablation of lesions, but it does not vaporize the tissue to the same extent as Er:YAG. It does, however, allow for collateral tissue damage in areas in which the ILVEN may be forming but is not yet clinically evident. It is for this reason we chose to use the laser in dual mode to address the minimally raised areas and the 2- to 3-mm perimeter around the affected skin. We then decreased the spot size from 4 mm to 2 mm to increase the fluence of Er:YAG (keeping CO₂ at 35%) and allow for focal ablative effects on the hyperkeratotic lesions. Attaining a balance between thorough ablation and hemostasis is possible by combining these laser modalities.

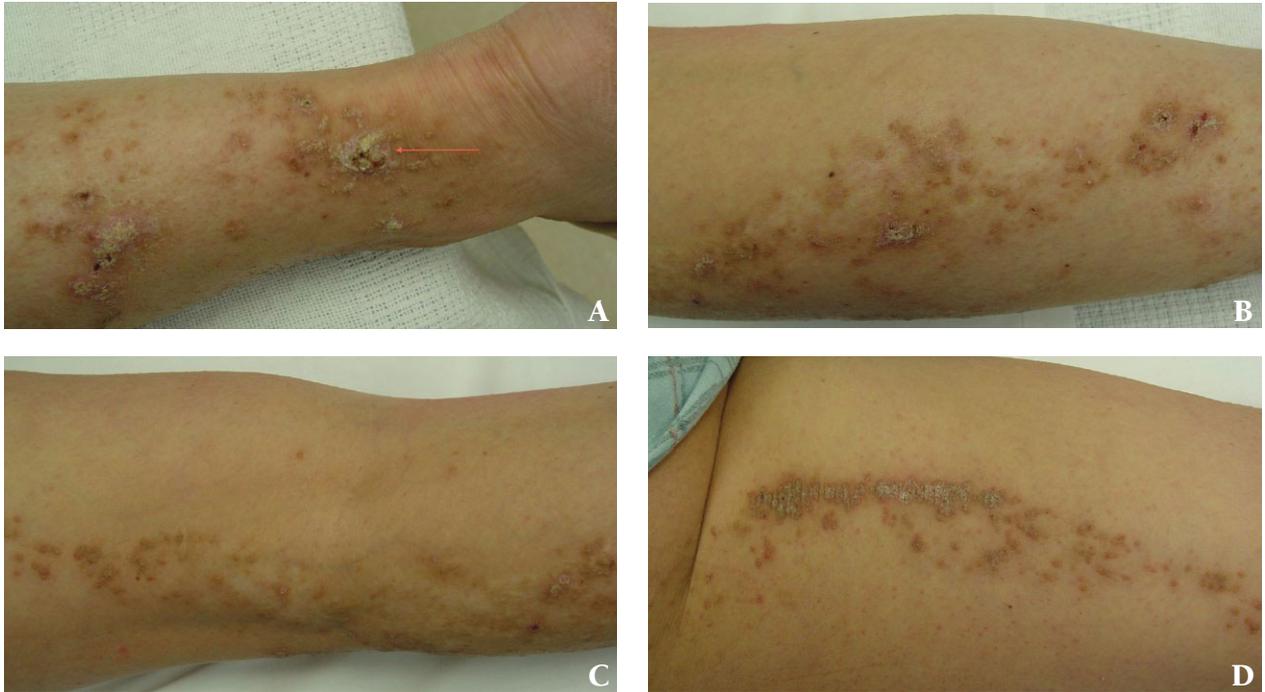


Figure 2. Baseline photos showing extensive linear verrucous papules and plaques extending along the entire length of her left posterior leg (A-D). Patient's most painful area is indicated by the red arrow (A).

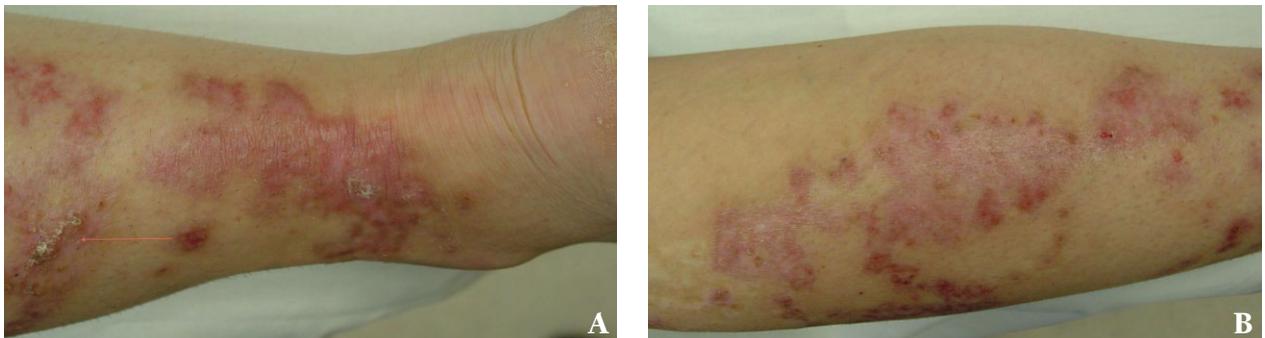


Figure 3. Verrucous papules and plaques have primarily resolved with postinflammatory erythema. There is evidence of slight recurrence in 1 area (A). Her most painful and hyperkeratotic area shows no evidence of recurrence (B).

CONCLUSION

Treatment of congenital lesions such as ILVEN, epidermal nevus, and nevus sebaceous remains a challenging problem. The physician must balance the desire for improvement with the risk of potential scarring when addressing these lesions. Factors that make these conditions difficult to treat include varying thickness, widespread distribution, and distribution over areas at higher risk for scarring (bony eminences, chest, and neck). Often the presentation for treatment is in early adolescence, which makes surgical excisions more risky as the patient's

body is undergoing significant growth and physical changes.

While topical and systemic therapies have shown variable results, they do play an important role in the maintenance of therapeutic response to ablative options. Therefore, patients should be encouraged to maintain their use until more definitive treatment options are found.

Our suggestion, based on the review of the literature and in our clinical practice, is to tailor the treatment to the patient depending on the area of involvement, the size of the lesions, the nature of the lesions (keratotic vs fleshy), and the thickness of the lesions.

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