

Inflammatory Linear Verrucous Epidermal Nevus Responsive to 308-nm Excimer Laser Treatment

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PRACTICE POINTS

- Inflammatory linear verrucous epidermal nevus (ILVEN) is a rare cutaneous disease that presents as linear psoriasiform plaques and associated prominent pruritus that can be refractory to treatment.
- Due to its clinical and histopathological similarities to psoriasis, ILVEN could potentially respond to psoriasis treatments.
- The excimer laser is ideal for inflammatory skin lesions because the UVB light induces apoptosis and can decrease keratinocyte proliferation.

Inflammatory linear verrucous epidermal nevus (ILVEN) is a rare cutaneous disease that presents as linear psoriasiform plaques with associated prominent pruritus. The lesions commonly present on the legs with onset during childhood. Inflammatory linear verrucous epidermal nevus typically is refractory to treatment. Therapies range from topical treatments to lasers and surgical options. It is clinically and histopathologically similar to psoriasis, suggesting it may respond to established psoriasis treatments such as the excimer laser. We report the case of an otherwise healthy 20-year-old woman with dry, pruritic, red lesions on the right leg that had been present since infancy. Biopsy revealed psoriasiform hyperplasia with a verruciform surface. Multiple topical treatments including ablative CO₂ laser therapy showed no remarkable improvement. The patient was then treated with a UV 308-nm excimer laser and showed noticeable clinical improvement. Because of its clinical and histopathological similarities to psoriasis, we hypothesized that the excimer laser may be useful in the treatment of these lesions.

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Inflammatory linear verrucous epidermal nevus (ILVEN) is a rare entity that presents with linear and pruritic psoriasiform plaques and most commonly occurs during childhood. It represents a dysregulation of keratinocytes exhibiting genetic mosaicism.^{1,2} Epidermal nevi may derive from keratinocytic, follicular, sebaceous, apocrine, or eccrine origin. Inflammatory linear verrucous epidermal nevus is classified under the keratinocytic type of epidermal nevus and represents approximately 6% of all epidermal nevi.³ The condition presents as erythematous and verrucous plaques along the lines of Blaschko.^{2,4} There is a predilection for the legs, and girls are 4 times more commonly affected than boys.¹ Cases of ILVEN are predominantly sporadic, though rare familial cases have been reported.⁴

Inflammatory linear verrucous epidermal nevus is notoriously refractory to treatment. First-line therapies include topical agents such as corticosteroids, calcipotriol, retinoids, and 5-fluorouracil.^{3,4} Other treatments include intralesional corticosteroids, cryotherapy, electrodesiccation and curettage, and surgical excision.³ Several case reports have shown promising results using the pulsed dye and ablative CO₂ lasers.⁵⁻⁸

Case Report

An otherwise healthy 20-year-old woman presented with dry, pruritic, red lesions on the right leg that had been present and stable since she was an infant (2 weeks of age). Her medical history included acne vulgaris, but she denied any personal or family history of psoriasis as well as any arthralgia or arthritis. Physical examination revealed discrete, oval, hyperkeratotic, scaly, red plaques on the lateral right leg with a larger hyperkeratotic, linear, red plaque extending from the right popliteal fossa to

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the posterior thigh (Figure 1A). The nails, scalp, buttocks, and upper extremities were unaffected. Bacterial culture of the right leg demonstrated *Staphylococcus aureus* colonization. Biopsy of the right popliteal fossa showed psoriasiform dermatitis with psoriasiform hyperplasia, a slightly verruciform surface, broad zones of superficial pallor, and parakeratosis with conspicuous colonies of bacteria (Figure 2).

Following the positive bacterial culture, the patient was treated with a short course of oral doxycycline, which did not alter the clinical appearance of the lesions or improve symptoms of pruritus. Pruritus improved moderately with topical corticosteroid treatment, but clinically the lesions appeared unchanged. The plaque on the superior right leg was treated with a superpulsed CO₂ laser and the plaque on the inferior right leg was treated with a fractional CO₂ laser, both with minimal improvement.

Because of the clinical and histopathologic similarities of the patient's lesions to psoriasis, a trial of the UV 308-nm excimer laser was initiated. Following initial test spots, she completed a total of 18 treatments to all lesions with noticeable clinical improvement (Figure 1B). Initially,

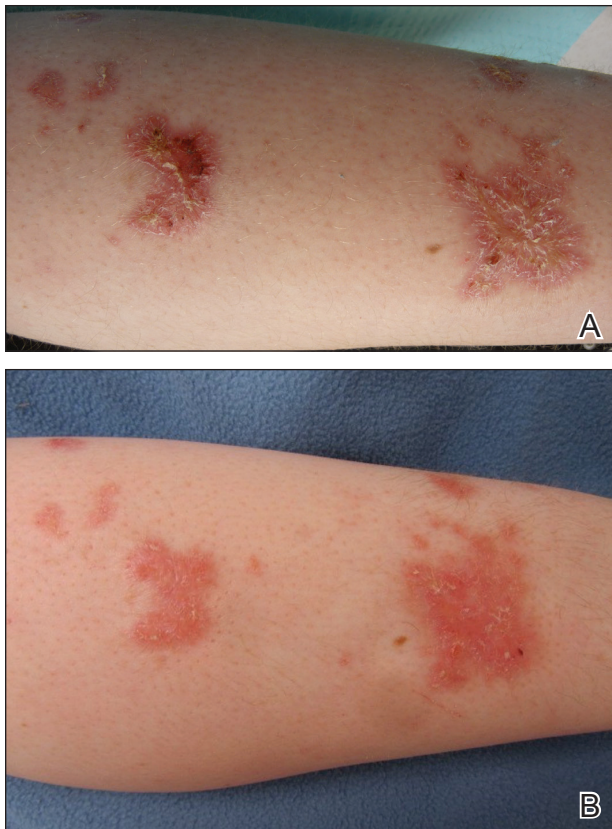


FIGURE 1. Inflammatory linear verrucous epidermal nevus lesions demonstrating discrete, hyperkeratotic, scaly, red plaques on the lateral right leg before (A) and after 18 treatment sessions with the 308-nm excimer laser (B). Improvement in hyperkeratotic scale and mild improvement in erythema was demonstrated.

the patient returned for treatment biweekly for approximately 5 weeks with 2 small spots being targeted at each session, with an average surface area of approximately 16 cm². She was started at 225 mJ/cm² with 25% increases at each session and ultimately reached up to 1676 mJ/cm² at the end of the 10 sessions. She tolerated the procedure well with some minor blistering. Treatment was deferred for 3 months due to the patient's schedule, then biweekly treatments resumed for 4 weeks, totaling 8 more sessions. At that time, all lesions on the right leg were targeted, with an average surface area of approximately 100 cm². The laser settings were initiated at 225 mJ/cm² with 20% increases at each session and ultimately reached 560 mJ/cm². The treatment was well tolerated throughout; however, the patient initially reported residual pruritus. The plaques continued to improve, and most notably, there was thinning of the hyperkeratotic scale of the plaques in addition to decreased erythema and complete resolution of pruritus. Ultimately, treatment was discontinued because of lack of insurance coverage and financial burden. The patient was lost to follow-up.

Comment

Presentation—Inflammatory linear verrucous epidermal nevus is a rare type of keratinocytic epidermal nevus⁴ that clinically presents as small, discrete, pruritic, scaly plaques coalescing into a linear plaque along the lines of Blaschko.⁹ Considerable pruritus and resistance to treatment are hallmarks of the disease.¹⁰ Histopathologically,

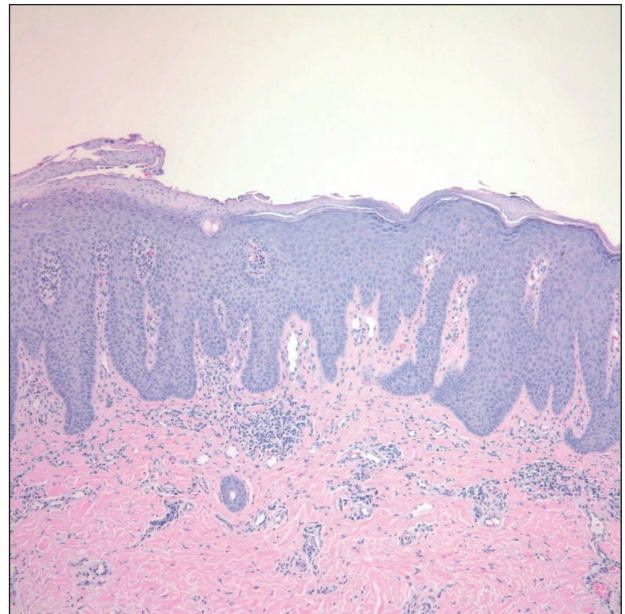


FIGURE 2. Uneven psoriasiform hyperplasia with a slightly verruciform surface, broad zones of superficial pallor, parakeratosis, focal hypergranulosis, vascular ectasia, and superficial perivascular and interstitial infiltrate of lymphocytes and plasma cells (H&E, original magnification ×10).

ILVEN is characterized by alternating orthokeratosis and parakeratosis with a lack of neutrophils in an acanthotic epidermis.¹¹⁻¹³ Inflammatory linear verrucous epidermal nevus presents at birth or in early childhood. Adult onset is rare.^{9,14} Approximately 75% of lesions present by 5 years of age, with a majority occurring within the first 6 months of life.¹⁵ The differential diagnosis includes linear psoriasis, epidermal nevi, linear lichen planus, linear verrucae, linear lichen simplex chronicus, and mycosis fungoides.^{4,11}

Differentiation From Psoriasis—Despite the histopathologic overlap with psoriasis, ILVEN exhibits fewer Ki-67–positive keratinocyte nuclei (proliferative marker) and more cytokeratin 10–positive cells (epidermal differentiation marker) than psoriasis.¹⁶ Furthermore, ILVEN has demonstrated fewer CD4⁺, CD8⁺, CD45RO⁺, CD2⁺, CD25⁺, CD94⁺, and CD161⁺ cells within the dermis and epidermis than psoriasis.¹⁶

The clinical presentations of ILVEN and psoriasis may be similar, as some patients with linear psoriasis also present with psoriatic plaques along the lines of Blaschko.¹⁷ Additionally, ILVEN may be a precursor to psoriasis. Altman and Mehregan¹ found that ILVEN patients who developed psoriasis did so in areas previously affected by ILVEN; however, they continued to distinguish the 2 pathologies as distinct entities. Another early report also hypothesized that the dermoepidermal defect caused by epidermal nevi provided a site for the development of psoriatic lesions because of the Koebner phenomenon.¹⁸

Patients with ILVEN also have been found to have extracutaneous manifestations and symptoms commonly seen in psoriasis patients. A 2012 retrospective review revealed that 37% (7/19) of patients with ILVEN also had psoriatic arthritis, cutaneous psoriatic lesions, and/or nail pitting. The authors concluded that ILVEN may lead to the onset of psoriasis later in life and may indicate an underlying psoriatic predisposition.¹⁹ Genetic theories also have been proposed, stating that ILVEN may be a mosaic of psoriasis² or that a postzygotic mutation leads to the predisposition for developing psoriasis.²⁰

Treatment—Inflammatory linear verrucous epidermal nevus frequently is refractory to treatment; however, the associated pruritus and distressing cosmesis make treatment attempts worthwhile.¹¹ No single therapy has been found to be successful in all patients. A widely used first-line treatment is topical or intralesional corticosteroids, with the former typically used with occlusion.¹³ Other treatments include adalimumab, calcipotriol,^{22,23} tretinoin,²⁴ and 5-fluorouracil.²⁴ Physical modalities such as cryotherapy, electrodesiccation, and dermabrasion have been reported with varying success.^{15,24} Surgical treatments include tangential²⁵ and full-thickness excisions.²⁶

The CO₂ laser also has demonstrated success. One study showed considerable improvement of pruritus and partial resolution of lesions only 5 weeks following

a single CO₂ laser treatment.⁵ Another study showed promising results when combining CO₂ pulsed laser therapy with fractional CO₂ laser treatment.⁶ Other laser therapies including the argon²⁷ and flashlamp-pumped pulsed dye lasers⁸ have been used with limited success. The use of light therapy and lasers in psoriasis have now increased the treatment options for ILVEN based on the rationale of their shared histopathologic characteristics. Photodynamic therapy also has been attempted because of its successful use in psoriasis patients. It has been found to be successful in diminishing ILVEN lesions and associated pruritus after a few weeks of therapy; however, treatment is limited by the associated pain and requirement for local anesthesia.²⁸

The excimer laser is a form of targeted phototherapy that emits monochromatic light at 308 nm.²⁹ It is ideal for inflammatory skin lesions because the UVB light induces apoptosis.³⁰ Psoriasis lesions treated with the excimer laser show a decrease in keratinocyte proliferation, which in turn reverses epidermal acanthosis and causes T-cell depletion due to upregulation of p53.^{29,31} This mechanism of action addresses the overproliferation of keratinocytes mediated by T cells in psoriasis and contributes to the success of excimer laser treatment.³¹ A considerable advantage is its localized treatment, resulting in lower cumulative doses of UVB and reducing the possible carcinogenic and phototoxic risks of whole-body phototherapy.³²

One study examined the antipruritic effects of the excimer laser following the treatment of epidermal hyperinnervation leading to intractable pruritus in patients with atopic dermatitis. The researchers suggested that a potential explanation for the antipruritic effect of the excimer laser may be secondary to nerve degeneration.³³ Additionally, low doses of UVB light also may inhibit mast cell degranulation and prevent histamine release, further supporting the antipruritic properties of excimer laser.³⁴

In our patient, failed treatment with other modalities led to trial of excimer laser therapy because of the overlapping clinical and histopathologic findings with psoriasis. Excimer laser improved the clinical appearance and overall texture of the ILVEN lesions and decreased pruritus. The reasons for treatment success may be twofold. By decreasing the number of keratinocytes and mast cells, the excimer laser may have improved the epidermal hyperplasia and pruritus in the ILVEN lesions. Alternatively, because the patient had ILVEN lesions since infancy, psoriasis may have developed in the location of the ILVEN lesions due to koebnerization, resulting in the clinical response to excimer therapy; however, she had no other clinical evidence of psoriasis.

Because of the recalcitrance of ILVEN lesions to conventional therapies, it is important to investigate therapies that may be of possible benefit. Our novel case documents successful use of the excimer laser in the treatment of ILVEN.

Conclusion

Our case of ILVEN in a woman that had been present since infancy highlights the disease pathology as well as a potential new treatment modality. The patient was refractory to first-line treatments and was concerned about the cosmetic appearance of the lesions. The patient was subsequently treated with a trial of a 308-nm excimer laser with clinical improvement of the lesions. It is possible that the similarity of ILVEN and psoriasis may have contributed to the clinical improvement in our patient, but the mechanism of action remains unknown. Due to the paucity of evidence regarding optimal treatment of ILVEN, the current case offers dermatologists an option for patients who are refractory to other treatments.

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