Inflammatory Linear Verrucous Epidermal Nevus: A Case Report and Short Review of the Literature

Amor Khachemoune, MD, CWS; Shahbaz A. Janjua, MD; Kjetil Kristoffer Guldbakke, MD

GOAL

To understand inflammatory linear verrucous epidermal nevus (ILVEN) to better manage patients with the condition

OBJECTIVES

Upon completion of this activity, dermatologists and general practitioners should be able to:

1. Describe the presenting characteristics of ILVEN.
2. Explain the differential diagnosis of ILVEN.
3. Discuss the treatment options for ILVEN.

CME Test on page 248.

This article has been peer reviewed and approved by Michael Fisher, MD, Professor of Medicine, Albert Einstein College of Medicine. Review date: September 2006.

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Drs. Khachemoune, Janjua, and Guldbakke report no conflict of interest. The authors discuss off-label use of 5-fluorouracil, acitretin, calcipotriol, corticosteroids, dithranol, pimecrolimus, and tretinoin. Dr. Fisher reports no conflict of interest.

Inflammatory linear verrucous epidermal nevus (ILVEN) is a unilateral, persistent, linear, pruritic eruption that usually appears on an extremity in infancy or childhood. We present a case of ILVEN in a 4-year-old boy and provide a short review of the literature, with emphasis on our current understanding of the etiology, clinical presentation, diagnosis, and management of ILVEN.

Cutis. 2006;78:261-267.

Accepted for publication November 28, 2005.

Dr. Khachemoune is Assistant Professor, Ronald O. Perelman Department of Dermatology, New York University School of Medicine, New York. Dr. Janjua is a specialist, Ayza Skin and Research Center, Lalamusa, Pakistan. Dr. Guldbakke currently is serving in the military in Norway.

Reprints: Amor Khachemoune, MD, CWS, Ronald O. Perelman Department of Dermatology, New York University School of Medicine, 530 First Ave, Suite 7R, New York, NY 10016 (e-mail: amorkh@pol.net).

Case Report

A 4-year-old boy presented for evaluation of an extremely pruritic linear plaque involving his right groin and right thigh since the age of one year (Figure 1). The plaque first appeared on the right buttock (Figure 2) and slowly enlarged, extending down spirally to involve the right inguinal region and upper inner thigh. There was no family history of similar dermatoses.

Results of a physical examination revealed multiple erythematous warty scaling papules coalesced to form a linear, verrucous, hyperpigmented plaque. The plaque extended from the right buttock and inguinal region to the right upper medial thigh following the lines of Blaschko. The rest of the physical examination results were unremarkable, and no associated physical anomaly was found. The eruption and the associated pruritus did not respond to either oral antihistamines or topical high potency steroids.

Results of a biopsy specimen taken from the lesion revealed hyperkeratosis, parakeratosis, acanthosis, and a decreased granular layer. A perivascular infiltrate of lymphocytes also was evident in the upper dermis. A diagnosis of inflammatory linear verrucous epidermal nevus (ILVEN) was made based on clinical and histopathologic grounds.

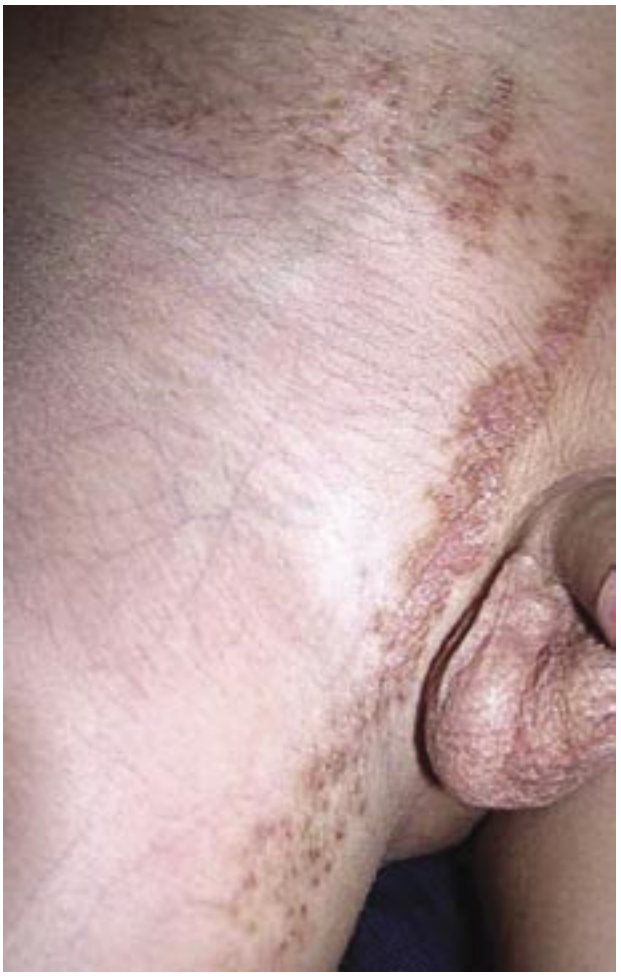

Figure 1. Well-demarcated erythematous scaly papules coalescing into a linear plaque involving the right groin and medial thigh.

Comment

The condition later known as *ILVEN* was first described by Unna in 1896.[1] However, it was not until 1971 that the disorder was described and clearly defined as a distinct entity by Altman and Mehregan[2] in a case series of 25 patients. The authors clearly delineated ILVEN as a clinical and histopathologic variety of linear verrucous nevus that clinically appears inflammatory and histopathologically appears psoriasiform.

The etiology of ILVEN remains unknown. It is considered a variant of keratinocytic epidermal nevus. Most cases are sporadic, but a familial case, with the condition occurring in a mother and her daughter, has been described.[3] Because ILVEN bears some histologic resemblance to psoriasis, some authors believe that the 2 conditions share a common pathogenesis, possibly mediated by cytokines.[4] There is some evidence that interleukins 1 and 6, tumor necrosis factor α, and intercellular adhesion molecule-1 are upregulated in ILVEN, similar to psoriasis.[4] It also has been proposed that activation of an autosomal-dominant lethal mutation that survives by mosaicism may be the cause. The mutated cells might survive in the vicinity of the normal cells.[5]

ILVEN usually appears in infancy or early childhood but may be present at birth; the condition is very rarely present in adulthood.[6] ILVEN occurs predominantly in females (female-male ratio, 4:1), and no racial predominance has been noted. About 6% of patients with epidermal nevi had ILVEN.[6]

ILVEN typically presents with multiple, discrete, erythematous, slightly warty and scaly papules that tend to coalesce into linear plaques. In a retrospective study of 23 patients with ILVEN, Lee and Rogers[7] documented a predilection for the buttock and legs, and most cases were unilateral. Onset usually was within the first 6 months of life, most patients (16 patients) were male, and extension beyond the original margins occurred in 6 patients (26%).[7]

Altman and Mehregan[2] described 6 characteristic features of ILVEN: (1) early age of onset, (2) predominance in females (4:1 female-male ratio), (3) frequent involvement of the left leg, (4) pruritus, (5) marked refractoriness to therapy, and (6) a distinctive psoriasiform and inflammatory histologic appearance.

In a few children, ILVEN has been found to occur in association with musculoskeletal or other abnormalities, including supernumerary digits and strabismus,[8] congenital bony anomalies of the ipsilateral extremities,[9] congenital dislocation of the ipsilateral hip and Fallot tetralogy of the heart,[10] autoimmune thyroiditis,[11] lichen amyloidosis,[12] nevus depigmentosus,[13] arthritis[14] and melanodontia.[15] More recently, ILVEN was associated with ipsilateral undescended testicle.[16] However, this finding was disputed by Happle,[17] who interpreted the case as an epidermal

Differential Diagnosis for Inflammatory Linear Verrucous Epidermal Nevus*

Condition	Population Group	Clinical Characteristics	Pathology	Therapy
Nevoid psoriasis in a Blaschko distribution	Usually children	Erythematous scaly plaques	Hyperkeratosis, parakeratosis, absence of granular cell layer, elongation of rete ridges, suprapapillary thinning, Munro microabscesses	Topical corticosteroids, vitamin D_3 analogues, systemic antipsoriatic medications, phototherapy
Epidermal nevi	Present at birth or during infancy	The lesion may be warty, smooth, or barely palpable of variable color±systemic abnormalities	Variable	Investigate for any associated features
Ichthyosiform nevus of CHILD syndrome	Infancy, female predominance	Unilateral, waxy, scaling erythematous plaques with a sharp midline demarcation±systemic abnormalities	Acanthosis with alternating orthokeratosis, parakeratosis, and patchy hypergranulosis	Emollients, topical keratolytics, management of any associated abnormality
Linear lichen planus	Mainly children	Violaceous, shiny, polygonal papules of varying sizes, often with prominent PIH	Irregular acanthosis, colloid bodies, bandlike infiltrate of lymphocytes and histiocytes in the upper dermis	Topical corticosteroids, antihistamines
Linear porokeratosis	Usually presents during childhood, no sex predilection	Grouped, linearly arranged, annular papules and plaques, with a raised peripheral ridge	Tightly packed parakeratotic cells in the coronoid lamella, lymphocytic infiltrate in the papillary dermis, central atrophy	Topical 5-fluorouracil, vitamin D_3 analogues, imiquimod, retinoids, close monitoring for malignant change
Nevoid BCC syndrome	Childhood/Early adolescence, no sex predilection	Multiple BCCs, pitting of palms and soles, jaw cysts±systemic abnormalities	Indistinguishable from BCC	Radiation, 5-fluorouracil, retinoids, PDT, surgery

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(continued)

Condition	Population Group	Clinical Characteristics	Pathology	Therapy
Basaloid follicular hamartoma	More common in children	Hypopigmented, smooth, or striaelike areas, with later appearance of pigmented papules and tumors, with or without or ulceration	Folliculocentered lesions with small basaloid cells admixed with squamous cells in a loose fibrous stroma	Close follow-up for any change in appearance
Linear lichen simplex chronicus	Usually in adults, more common in women	Erythematous, scaly, well-demarcated, lichenified, firm, rough plaques with exaggerated skin lines	Hyperkeratosis, acanthosis, spongiosis, patches of parakeratosis, papillary dermal fibrosis	Topical corticosteroids, tacrolimus, antianxiety medications
Linear keratosis follicularis	Any age, more common in children; no sex predilection	Keratotic, sometimes crusted, red to brown papules in a linear arrangement	Acantholysis with suprabasilar cleft formation and dyskeratosis	Topical corticosteroids, retinoids, immunosuppressive agents, surgery
Linear lichen nitidus	Most common in childhood/early adolescence, no sex predilection	Multiple 1- to 3-mm, sharply demarcated, round or polygonal, flat-topped, skin-colored shiny papules	Flattened epidermis with parakeratosis, dermal lymphohistiocytic inflammatory infiltrate	Topical corticosteroids, retinoids, phototherapy
Linear warts	More common in children, no sex predilection	Hyperkeratotic papules with a rough irregular surface	Digitated epidermal hyperplasia, acanthosis, papillomatosis, compact orthokeratosis, hypergranulosis	Topical keratolytics, imiquimod, intralesional bleomycin, cryotherapy
Mycosis fungoides	Not established	Localized linear pruritic verrucous confluent papules and plaques	Pautrier microabscesses, follicular epitheliotropism	RePUVA

*CHILD indicates congenital hemidysplasia with ichthyosiform erythroderma and limb defects; PIH, postinflammatory hyperpigmentation; BCC, basal cell carcinoma; PDT, photodynamic therapy; RePUVA, re-treatment with psoralen plus UVA.

nevus of the epidermolytic type and stated that the ipsilateral cryptorchidism should be considered as a coincidental finding.

The histopathologic presentation of ILVEN is very similar to psoriasis. Results of a histologic examination reveal psoriasiform hyperplasia of the epidermis, alternating parakeratosis without a granular layer, and orthokeratosis with a thickened granular layer.[18] The authors of a recent study[19] looked at advanced immunohistochemical methods

to differentiate ILVEN from psoriasis. The investigators found that the number of Ki-67–positive nuclei tends to be lower, and the number of keratin-10–positive cells and HLA-DR expression tend to be higher in patients with ILVEN. The density of $CD8^+$, $CD45RO^+$, $CD2^+$, CD94, and CD161 also showed a marked difference between ILVEN and psoriasis. In addition, the number of T cells relevant in the pathogenesis of psoriasis was markedly reduced in ILVEN.[19]

Other dermatoses that need to be differentiated from ILVEN are summarized in the Table. Nevoid psoriasis in a Blaschko distribution closely mimics ILVEN, but the former usually is asymptomatic and responds well to antipsoriatic treatment. Psoriasis also may become superimposed on an epidermal nevus because of Köbnerization.[20]

Epidermal nevi may occur almost anywhere on the head, neck, legs, or trunk.[6] Nevus verrucosus is a term for the localized lesions of epidermal nevi.[21] Linear verrucous epidermal nevi are linear hamartomas of epidermal structures that usually appear at birth or during infancy. Linear verrucous epidermal nevi usually are found on the lower extremities and have resistance to treatment and risk of recurrence. The nevi rarely are seen on the face and very rarely involve the oral mucosa.[21] Clinically, there is no erythema or pruritus. Immunohistochemical studies further help differentiate ILVEN from other noninflammatory linear epidermal nevi.

The CHILD syndrome (congenital hemidysplasia with ichthyosiform erythroderma and limb defects) is characterized by segmentally distributed asymptomatic erythematous verrucous areas, associated with ipsilateral extremity defects, ranging from digital hypoplasia to agenesis of the extremity.[22] Hence, ILVEN reported in association with severe extremity defects is most likely CHILD syndrome.[23] An alternative acronym that has been used to describe this association is PENCIL (psoriasiform epidermal nevus with congenital ipsilateral limb defects).[24]

Lichen striatus usually is asymptomatic and resolves spontaneously. There also are histologic differences between ILVEN and lichen striatus.[25] Linear lichen planus mainly affects children and is characterized by discrete pruritic, polygonal, violaceous papules arranged in a linear fashion, usually along an entire extremity; however, the papules also may be zosteriform.[26]

Linear porokeratosis also usually presents during childhood as ringlike, hypertrophic, verrucous plaques with a linear morphology, usually on a single extremity, but other parts of the body also may be involved.[27] More recently, Jang et al[28] reported a case of mycosis fungoides, presenting with a clinical picture of ILVEN.

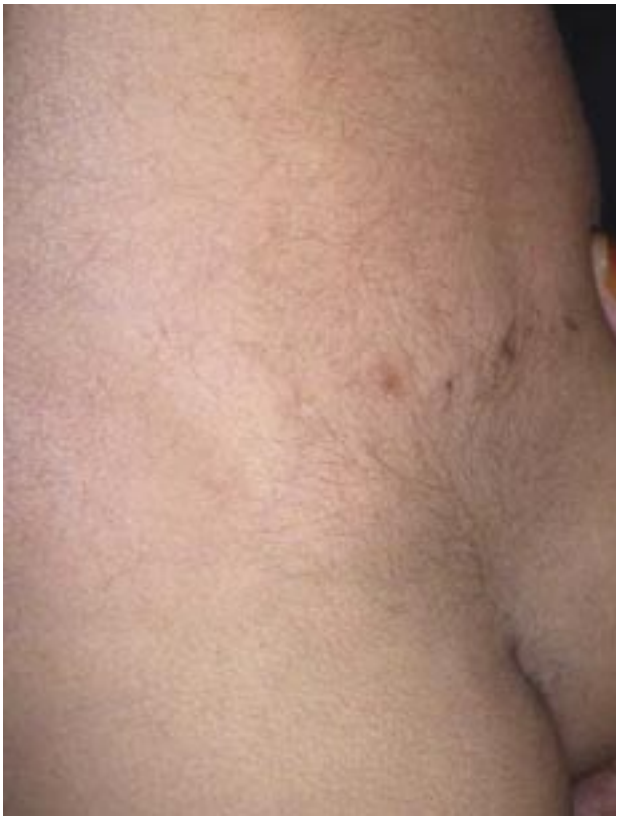

Figure 2. Involvement of the right buttock and right lower back.

Nevoid basal cell carcinoma (BCC) syndrome is characterized by BCCs in both sun-exposed and nonexposed skin. The diameter of the lesions varies from 1 to 10 mm and commonly involves the face, back, and chest. Features such as odontogenic cysts, palmar and plantar pitting, and facial milia may be associated.

Basaloid follicular hamartoma, also known as linear unilateral basal cell nevus with comedones, may present as a unilateral linear lesion.[29] In its early stages, the lesion shows hypopigmented smooth or striaelike areas, which later may develop darker-pigmented papules and tumors with or without ulceration. Of note, it may be histologically indistinguishable from the infundibulocystic type of BCC.[29]

The most widely applied medical treatments for ILVEN have been intralesional corticosteroids or potent topical corticosteroids, the latter often with occlusion.[30] However, the clinical appearance and associated intense pruritus usually are refractory to treatment. Topical calcipotriol has been reported to provide some relief in some patients,[31] but it is not recommended in children because of limited clinical safety data. A recent case report noted improvement of pruritus in ILVEN with topical pimecrolimus

cream.[32] Dithranol has been used with success in one case report,[33] but this has been interpreted as an antipsoriatic effect in ILVEN with superimposed psoriasis.[34] Other therapeutic choices reported in the literature include topical tretinoin combined with 5-fluorouracil,[35] and acitretin.[36]

Destructive therapies, such as the application of liquid nitrogen, electrodesiccation, ablative laser and dermabrasion, have all been equally disappointing.[37] Of note, case reports have shown efficacy of CO_2[38] and pulsed dye laser treatment.[39]

Conclusion

ILVEN may be an isolated finding or may be associated with other abnormalities. Most patients present in infancy or early childhood. The diagnosis may sometimes be difficult and necessitate biopsy and advanced immunohistochemical analysis. Most lesions do not persist and spontaneously resolve by adulthood.[40] The management usually is only symptomatic and often unsatisfactory.

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