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

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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.


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 (IL VEN) was made based on clinical and histopathologic grounds.

Comment

The condition later known as ILVEN was first described by Unna in 1896. However, it was not until 1971 that the disorder was described and clearly defined as a distinct entity by Altman and Mehregan 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. Because ILVEN bears some histologic resemblance to psoriasis, some authors believe that the 2 conditions share a common pathogenesis, possibly mediated by cytokines. 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. 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.

ILVEN usually appears in infancy or early childhood but may be present at birth; the condition is very rarely present in adulthood. 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.

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 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%).

Altman and Mehregan 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, congenital bony anomalies of the ipsilateral extremities, congenital dislocation of the ipsilateral hip and Fallot tetralogy of the heart, autoimmune thyroiditis, lichen amyloidosis, nevus depigmentosus, arthritis and melanodontia. More recently, ILVEN was associated with ipsilateral undescended testicle. However, this finding was disputed by Happle, who interpreted the case as an epidermal
<table>
<thead>
<tr>
<th>Condition</th>
<th>Population Group</th>
<th>Clinical Characteristics</th>
<th>Pathology</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nevoid psoriasis in a Blaschko distribution</td>
<td>Usually children</td>
<td>Erythematous scaly plaques</td>
<td>Hyperkeratosis, parakeratosis, absence of granular cell layer, elongation of rete ridges, suprapapillary thinning, Munro microabscesses</td>
<td>Topical corticosteroids, vitamin D analogues, systemic antipsoriatic medications, phototherapy</td>
</tr>
<tr>
<td>Epidermal nevi</td>
<td>Present at birth or during infancy</td>
<td>The lesion may be warty, smooth, or barely palpable of variable color±systemic abnormalities</td>
<td>Variable</td>
<td>Investigate for any associated features</td>
</tr>
<tr>
<td>Ichthyosiform nevus of CHILD syndrome</td>
<td>Infancy, female predominance</td>
<td>Unilateral, waxy, scaling erythematous plaques with a sharp midline demarcation±systemic abnormalities</td>
<td>Acanthosis with alternating orthokeratosis, parakeratosis, and patchy hypergranulosis</td>
<td>Emollients, topical keratolytics, management of any associated abnormality</td>
</tr>
<tr>
<td>Linear lichen planus</td>
<td>Mainly children</td>
<td>Violaceous, shiny, polygonal papules of varying sizes, often with prominent PIH</td>
<td>Irregular acanthosis, colloid bodies, bandlike infiltrate of lymphocytes and histiocytes in the upper dermis</td>
<td>Topical corticosteroids, antihistamines</td>
</tr>
<tr>
<td>Linear porokeratosis</td>
<td>Usually presents during childhood, no sex predilection</td>
<td>Grouped, linearly arranged, annular papules and plaques, with a raised peripheral ridge</td>
<td>Tightly packed parakeratotic cells in the coronoid lamella, lymphocytic infiltrate in the papillary dermis, central atrophy</td>
<td>Topical 5-fluorouracil, vitamin D analogues, imiquimod, retinoids, close monitoring for malignant change</td>
</tr>
<tr>
<td>Nevoid BCC syndrome</td>
<td>Childhood/Early adolescence, no sex predilection</td>
<td>Multiple BCCs, pitting of palms and soles, jaw cysts±systemic abnormalities</td>
<td>Indistinguishable from BCC</td>
<td>Radiation, 5-fluorouracil, retinoids, PDT, surgery</td>
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</tbody>
</table>

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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. The authors of a recent study looked at advanced immunohistochemical methods.
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to differentiate IL VEN 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 IL VEN. The density of CD8+, CD45RO+, CD2+, CD94, and CD161 also showed a marked difference between IL VEN and psoriasis. In addition, the number of T cells relevant in the pathogenesis of psoriasis was markedly reduced in IL VEN.

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

Epidermal nevi may occur almost anywhere on the head, neck, legs, or trunk. Nevus verrucosus is a term for the localized lesions of epidermal nevi. 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. Clinically, there is no erythema or pruritus. Immunohistochemical studies further help differentiate IL VEN 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. Hence, IL VEN reported in association with severe extremity defects is most likely CHILD syndrome. An alternative acronym that has been used to describe this association is PENCIL (psoriasisform epidermal nevus with congenital ipsilateral limb defects).

Lichen striatus usually is asymptomatic and resolves spontaneously. There also are histologic differences between IL VEN and lichen striatus. 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.

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. More recently, Jang et al reported a case of mycosis fungoides, presenting with a clinical picture of IL VEN.

Nevoid basal cell carcinoma (BCC) syndrome is characterized by BCCs in both sun-exposed and non-exposed 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. In its early stages, the lesion shows hypopigmented smooth or striate-like 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.

The most widely applied medical treatments for IL VEN have been intrallesional corticosteroids or potent topical corticosteroids, the latter often with occlusion. 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, but it is not recommended in children because of limited clinical safety data. A recent case report noted improvement of pruritus in IL VEN with topical pimecrolimus.

Figure 2. Involvement of the right buttock and right lower back.
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cream. Dithranol has been used with success in one case report, but this has been interpreted as an antipsoriatic effect in ILVEN with superimposed psoriasis. Other therapeutic choices reported in the literature include topical tretinoin combined with 5-fluorouracil, and acitretin.

Destructive therapies, such as the application of liquid nitrogen, electrodesiccation, ablative laser and dermabrasion, have all been equally disappointing. Of note, case reports have shown efficacy of CO$_2$ and pulsed dye laser treatment.

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. The management usually is only symptomatic and often unsatisfactory.

REFERENCES