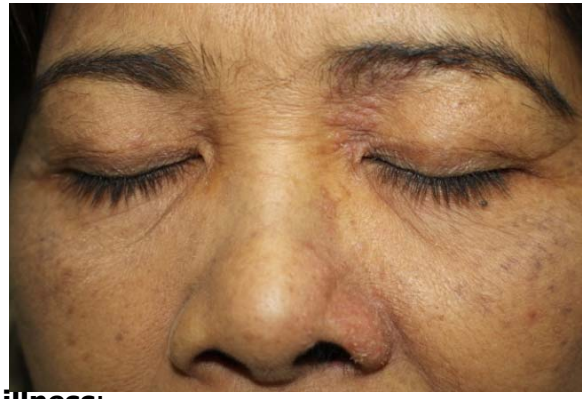
Case 15
A 60 year-old Thai woman from Ayutthaya
Chief complaint: Multiple pruritic papules on left alar nasi for 10 years



Present illness:
The patient developed multiple scaly erythematous papules with marked pruritus on her left alar nasi for 10 years. The lesions gradually extended to the left medial canthus and left upper eyelid. She was treated with topical mometasone cream with limited improvement. She was otherwise in good health
Past history: Anemia

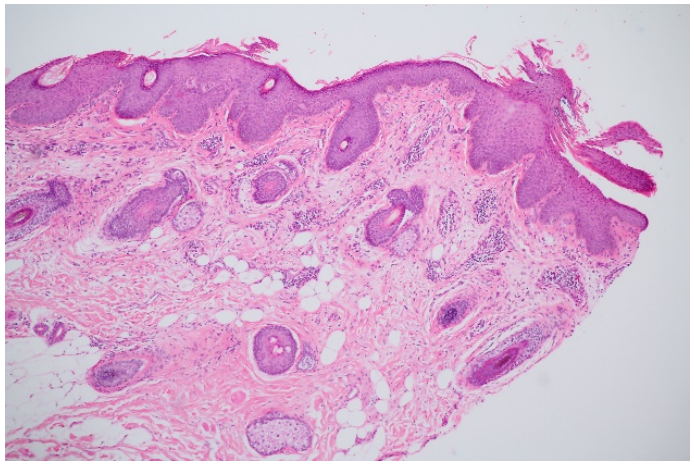
Family history:
There was no family history of similar cutaneous lesions

Skin examination:
Multiple ill-defined scaly erythematous papules on left medial canthus, upper eyelid extending to left alar nasi

Physical examination:
Systemic examination other than skin lesions revealed no abnormality

Laboratory investigation:
KOH: negative

Histopathology: (S16-6817A, left eyelid)



- Alternating para/orthokeratosis and hypo/hypergranulosis in the stratum corneum and psoriasiform epidermal hyperplasia
- Superficial perivascular infiltrate of lymphocytes

Diagnosis: Inflammatory linear verrucous epidermal nevus

Treatment:
- Topical calcipotriol/betamethasone gel applied once daily

- Cream base applied twice daily
- Cetirizine (10 mg) 1 tab oral twice daily
- Hydroxyzine (10 mg) 1 tab oral at bedtime
- Plan for CO_2 laser treatment

Presenter: Nongsak Chanasumon, MD
Consultant: Penpun Wattanakrai, MD

Discussion:

Inflammatory linear verrucous epidermal nevus (ILVEN) is a relatively rare variant (accounted for 6%) of verrucous epidermal nevus which is a harmatomatous proliferation of the epithelium. It was originally described by Altman and Mehregan in 1971.[1]It is a linear, psoriasiform, erythematous, scaly papule or plaque that follows Blaschko's lines, unilaterally with more affected on the left side and is characteristically pruritic.[1] It usually appears during childhood with 75% of nevi appearing before the age of 5 years, however late onset in adults has also been reported.[2] It predominates in females in the ratio of 4:1.[1] Most cases are sporadic, although familial cases have been described.[3,4,5] The distribution was predominantly on the lower half of the body, especially on buttock area,[1,6] and is relatively rare on genital and perigenital area.[6,7] Only 16% of lesions were found on the upper half of the body, including the axillae, arm, and hand.[6] There was one case report of ILVEN located on right upper eyelid[8] In our case, the lesions are located on the face including left upper eyelid, medial canthus and alar nasi which are unusual sites.

An estimated one-third of individuals with epidermal nevi have involvement of other organ systems especially ophthalmic, neurologic and skeletal system; called epidermal nevus syndrome, however it is seldom reported in ILVEN. Rarely, there are ipsilateral skeletal abnormalities, usually reduction deformities, suggesting that ILVEN is possibly a forme fruste of CHILD syndrome.[9] ILVEN had also been reported in association with regional odontodysplasia[10], arthritis[11], autoimmune lymphocytic thyroiditis[12], hereditary mucinous nevus[13], undescended testis[14], and lichen amyloidosis[15]. Moreover, there was one case report of malignant transformation of ILVEN into squamous cell carcinoma.[16] In this case no other organ abnormalities or malignancy change was observed.

Inflammatory linear verrucous epidermal nevus is caused by somatic mutations that result in genetic mosaicism and although its physiopathology is still unclear, it is believed that it may be associated with an increase in the production of interleukins-1 and 6, tumor necrosis factor-alpha, and intercellular adhesion molecule.

The differential diagnosis of ILVEN includes other various dermatoses such as Darier's disease, linear porokeratosis, linear lichen planus, linear psoriasis, and lichen striatus.

Skin biopsy is crucial in the diagnosis of ILVEN. There are two different histopathological features for ILVEN: nonspecific and specific. Areas of depressed hypergranulosis and overlying orthokeratosis alternating sharply with areas of agranulosis and overlying parakeratosis are specific features, but are not pathognomonic.[17,18]The nonspecific findings includes an inflammatory dermal infiltrate, acanthosis, and papillomatosis of the psoriasis type with elongation of the epidermal ridges.[17]

ILVEN is markedly refractory to therapy. Topical treatments such as topical corticosteroids with or without occlusion, intralesional steroid injections, and topical retinoids are rarely beneficial. Vitamin D analogs, as well as combination of potent topical steroid and topical calcineurin inhibitor, and medium to full-depth chemical peels were found to be helpful in some cases.[19,20,21,22] There are few reports of effective systemic treatments with acitretin and etanercept.[23,24] Among the physical modalities; cryotherapy, photodynamic therapy, carbon dioxide laser therapy, and 585 nm flashlamp-pumped pulsed dye laser have

been tried successfully.[25,26,27] Although surgical excision tends to be followed by rapid recurrence and requires a generous depth of underlying dermis to be removed, there were some reported cases successfully treated with full-thickness surgical excision.[18,28]

References

1. Altman J, Mehregan AH. Inflammatory linear verrucous epidermal nevus. Arch Dermatol 1971;104:385–9.
2. Kawaguchi H, Takeuchi M, Ono H , Nakajima H. Adult onset of inflammatory linear verrucous epidermal nevus. J Dermatol 1999;26:599.
3. Hamm H, Happle R. Inflammatory linear verrucous epidermal nevus (ILVEN) in a mother and her daughter. Am J Med Genet 1986;24:685–90.
4. Goldman K, Don PC. Adult onset of inflammatory linear epidermal nevus in a mother and her daughter. Dermatology 1994;189:170–2.
5. Mazereeuw-Hautier J, Marty C, Bonafe JL. Familial inflammatory linear verrucous epidermal naevus in a father and daughter. Clin Exp Dermatol 2008;33:679-80.
6. Rogers M. Epidermal nevi and the epidermal nevus syndromes: A review of 233 cases. Pediatr Dermatol 1992;9:342–4.
7. Bandyopadhyay D, Saha A. Genital/Perigenital Inflammatory Linear Verrucous Epidermal Nevus: A Case Series. Indian J Dermatol 2015;60:592-5.
8. Nakai N, Ohshita A, Katoh N. A Case of Inflammatory Linear Verrucous Epidermal Nevus on the Upper Eyelid. Indian J Dermatol 2015;60:323-4.
9. Moss C, Burn J. CHILD + ILVEN = PEN or PENCIL. J Med Genet 1990;27:390–1.
10. Prakash SMR, Gupta S, Kamarthi N , Goel S. Inflammatory linear verrucous epidermal nevus and regional odontodysplasia: A rare sorority. Indian J Dent 2015;6:203-6.
11. Al-Enezi S, Huber AM, Krafchik BR, Laxer RM. Inflammatory linear verrucous epidermal nevus and arthritis: A new association. J Pediatr 2001;138:602–4.
12. Dereure O, Paillet C, Bonnel F, Guilhou JJ. Inflammatory linear verrucous epidermal naevus with auto-immune thyroiditis: coexistence of two auto-immune epithelial inflammations? Acta Derm Venereol 1994;74:208-9.
13. Vukicevic JS, Milobratovic DJ, Milinkovic MV , Bogdanovic Z. Extensive, adulthood inflammatory linear verrucous epidermal nevus associated with mucinous nevus. Indian J Dermatol 2011;77:607-8.
14. Oskay T , Kutluay L. Inflammatory linear verrucous epidermal naevus associated with ipsilateral undescended testicle. Clin Exp Dermatol 2003;28:557-8.
15. Zhuang L, Wenyuan Z. Inflammatory linear verrucous epidermal nevus coexisting with lichen amyloidosis. J Dermatol 1996;23:415.
16. Turk BG, Ertam I, Urkmez A, Kazandi A, Kandiloglu G , Ozdemir F. Development of squamous cell carcinoma on an inflammatory linear verrucous epidermal nevus in the genital area. Cutis 2012;89:273-5.
17. Vissers WH, Muys L, Van Erp PE, de Jong EM, van de Kerkhof PC. Immunohistochemical differentiation between inflammatory linear verrucous epidermal nevus (ILVEN) and psoriasis. Eur J Dermatol 2004;14:216–20.
18. Lee BJ, Mancini AJ, Renucci J, Paller AS, Bauer BS. Full-thickness surgical excision for the treatment of inflammatory linear verrucous epidermal nevus. Ann Plast Surg 2001;47:285–92.
19. Zvulunov A, Grunwald MH, Halvy S. Topical calcipotriol for treatment of inflammatory linear verrucous epidermal nevus.

Arch Dermatol 1997;133:567–8.
20. Mitsuhashi Y, Katagiri Y, Kondo S. Treatment of inflammatory linear verrucous epidermal naevus with topical vitamin D3. Br J Dermatol 1997;136:134–5.
21. Bohm M, Luger TA, Traupe H. Successful treatment of inflammatory linear verrucous epidermal naevus with topical natural vitamin D3 (calcitriol). Br J dermatol 2003;148:824-5.
22. Mutasim DF. Successful treatment of inflammatory linear verrucous epidermal nevus with tacrolimus and fluocinonide. J Cutan Med Surg 2006;10:45-7.
23. Renner R, Rytter M, Sticherling M. Acitretin treatment of a systematized inflamatory linear verrucous epidermal naevus. Acta Derm Venereol 2005;85:348–50.
24. Bogle MA, Sobell JM, Dover JS. Successful treatment of a widespread inflammatory verrucous epidermal nevus with etanercept. Arch Dermatol 2006;142:401–2.
25. Parera E, Gallardo F, Toll A, Gil I, Sánchez-Schmidt J, Pujol R. Inflammatory linear verrucous epidermal nevus successfully treated with methyl-aminolevulinate photodynamic therapy. Dermatol Surg 2010;36:253–6.
26. D'Antuono A, Balestri R, Zauli S, Bardazzi F, Bellavista S, Banzola N, et al. Carbon dioxide laser: First-line therapy in vulvar inflammatory linear verrucous epidermal nevus. Dermatol Ther 2012;25:92–4.
27. Alster TS. Inflammatory linear verrucous epidermal nevus: successful treatment with the 585 nm flashlamp-pumped pulsed dye laser. J Am Acad Dermatol 1994;31:513-4.
28. Behera B, Devi B, Nayak BB, Sahu B, Singh B , Puhan MR. Giant Inflammatory Linear Verrucous Epidermal Nevus: Successfully Treated with Full Thickness Excision and Skin Grafting. Indian J Dermatol 2013;58:461-3.