# Ichthyosis Linearis Circumflexa

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**The authors present a 3-year-old boy showing generalized migratory erythema with double-edged scaling borders since 3 months after birth. Histologic examination revealed an acanthotic epidermis with hyperkeratosis, focal parakeratosis and papillomatosis. The PAS-positive, diastase-resistant, amorphous materials were found in the space of parakeratotic scales and cytoplasms of spinous cells just below the parakeratotic lesion. On electron microscopy, we could observe the round dense bodies in the upper spinous cells and a number of lipoid granules in the horny layer.**

**Our patient showed characteristic clinical, microscopic and ultrastructural features of ichthyosis linearis circumflexa(ILC). However, he showed no hair shaft abnormalities, which is the common finding of Netherthon's syndrome(NS) along with ILC and atopic diathesis. (Ann Dermatol 8:(1)51~56, 1996).**

*Key Words* : Ichthyosis Linearis Circumflexa, Electron Microscopic Findings

Ichthyosis linearis circumflexa(ILC) is a rare, autosomal recessive inherited genodermatosis, and usually occurs at birth or during the first year of life. It is characterized by migratory polycyclic serpiginous erythema, often with peripheral double-edged scaling border. It may undergo exacerbations and remissions, but complete clearing does not occur[1,2]. Many reports have revealed ILC with atopic diathesis and various types of hair shaft abnormalities as Netherton's syndrome[2-6].

The term ILC was first coined by Cômel[7] in 1949 to describe a previously unreported ichthyosiform dermatosis. Many authors, however, gave credit to Netherton[3], who described a patient with ILC and bamboo hair(trichorrhexis invaginata). Since then it has been more clearly defined, and most of the cases earlier reported had defects of the hair shaft[8].

We describe a case of ILC which showed characteristic clinical, microscopic and ultrastructural features, but no hair shaft abnormalities have yet been found.

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## REPORT OF A CASE

A 3-year-old boy visited our clinic with generalized erythematous scaling skin lesions that had been present since 3 months after birth. He was born after normal gestation and delivery, and he was healthy except his skin eruption. The lesions were first seen in the trunk area, and gradually extended to become generalized giving rise to migratory figurated scaly erythema with mild itching. The lesions were located predominantly over the trunk and proximal extremities. Periodic exacerbations and remissions were noted without complete clearing of the skin lesions. Exacebation seemed to be more frequent in winter time, while in summer the lesions tended to improve and be localized at proximal extremities. Past history revealed nothing contributory. There were no family history of consanguinity or of similar skin lesion, and neither familial nor personal history of asthma, hay fever, eczema, urticaria, angioedema were noted.

On physical examination, symmetrically distrib-

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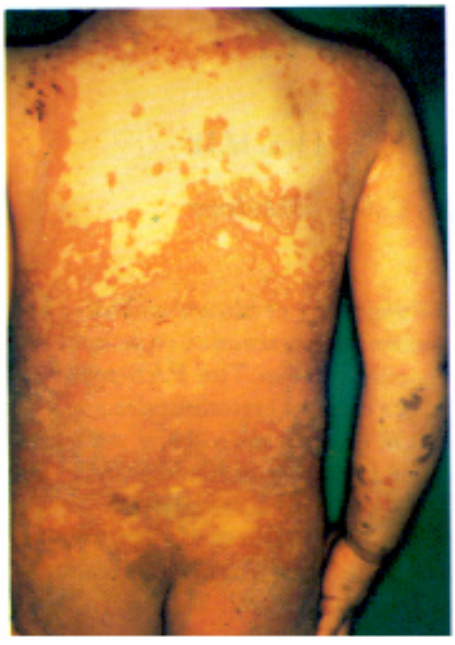

Fig. 1. Erythematour polycyclic scaling eruption on back, buttock and extremities.

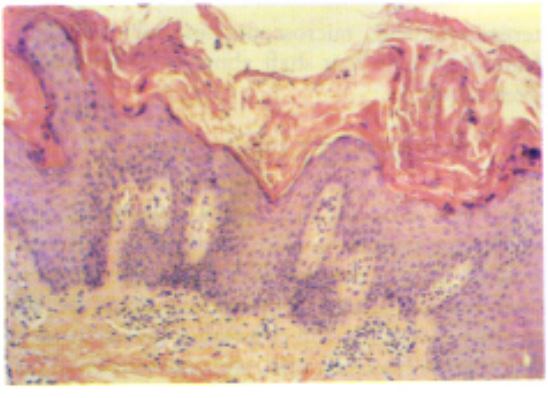

Fig. 3. Epidermis shows papillomatosis, hyperkeratosis, focal parakeratosis and acanthosis with normal or absent granular layer. In the upper dermis, moderate perivascular lymphohistiocytic infiltration and capillary proliferation are seen(H & E stain, ×40).

uted generalized erythematous scaling eruption with polycyclic serpiginous margin was observed most markedly on the trunk, buttock and proximal extremities(Fig.1). The erythema presented a relatively well demarcated margin often showing double-edged scaling borders(Fig.2). The face and eyelids were diffusely red and scaly, and severe lichenification and hyperpigmentation were found in the flexoral folds including antecubital fossae,

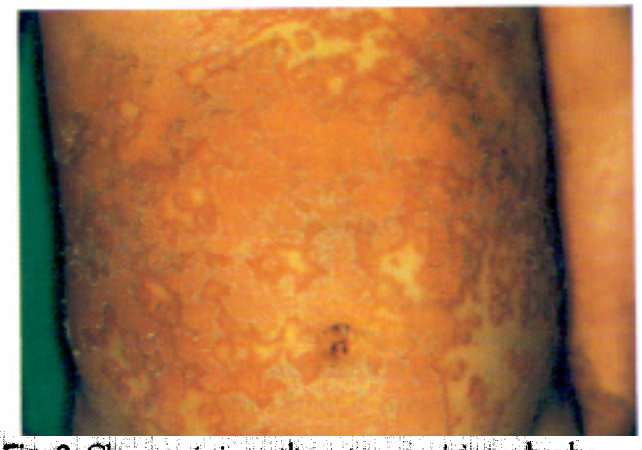

Fig. 2. Characteristic erythematous serpiginous border with peripheral double-edged scale on abdominal lesion.

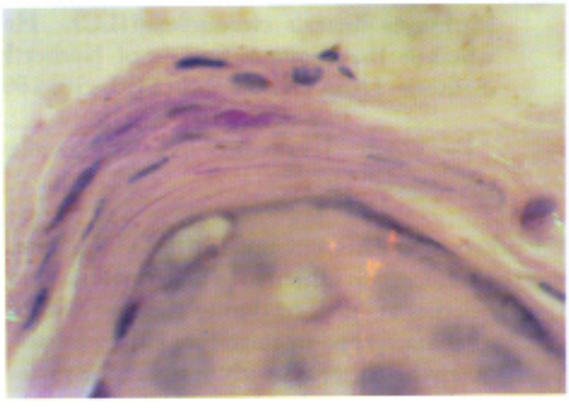

Fig. 4. The PAS-positive, diastase-resistant, eosinophilic homogenous amorphous materials in parakeratotic stratum corneum, known as glycolipoprotein (PAS stain, ×400).

nape of the neck and dorsa of the hands and feet. No abnormalities in the mucous membrane, teeth or nails were seen. Hair plucked from scalp, eyebrows and eyelashs revealed no apparent abnomalities on repeated microscopic examination.

Laboratory data including CBC, Eosinophil and lymphocytes subset test were within normal values. In MAST allergy test, total IgE was moderately elevated (class 2 ; 1.78 Volts) and D.P., D.F. was strongly positive. There were an increase of glutamic acid( 92 μmol/day, reference value:20-50 μmol/day) and proline(Trace, reference value : no detection) in 24 hour collected urine.

Skin biopsy specimens were taken from the active border of the buttock and left upper arm. H&E staining showed acanthotic epidermis with hyperk-

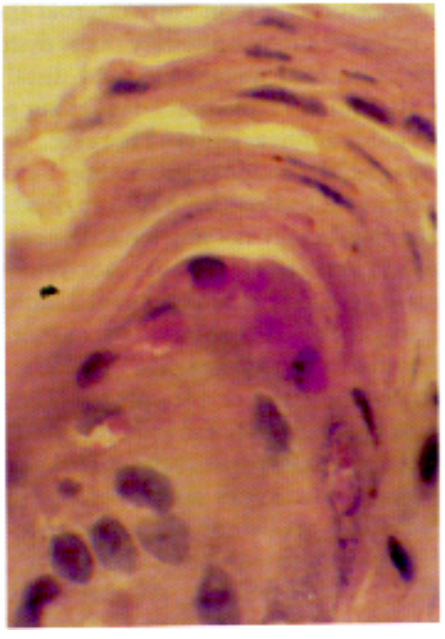

Fig. 5. Focal accumulations of PAS-positive, diastase-resistant, materials in the upper spinous layer just below the parakeratotic horny layerjust below the parakeratotic horny layer(PAS stain, ×400).

eratosis, focal parakeratosis and papillomatosis. The granular layer was normal or absent in some areas(Fig.3). The parakeratotic epidermis seemed to be loose, and the cytoplasms of the upper prickle cells beneath the parakeratotic area had intracytoplasmic vacuoles, which occasionally seemed to fill up the whole cell body. The papillary dermis showed an infiltrate mainly composed of lymphohistiocytes, and the capillaries were moderately dilated. In PAS staining, somewhat loosely arranged parakeratotic stratum corneum showed focal accumulations of PAS-positive, diasrase-resistant, eosinophilic amorphous materials(Fig.4). In some areas, just below the parakeratotic lesion the PAS-positive, homogenous eosinophilc materials also showed(Fig.5). Alcian blue stain was negative. On electron microscopic examination, the main alteration of the affected upper spinous cells was the presence of round or oval cytoplasmic dense bodies(Fig.6). Their diameter varied from 0.5 up to 2 ㎛ or more. At higher magnification view, they appeared to be formed by a amorphous, finely granular substance. The Golgi apparatus and endoplasmic reticulum were normally developed, and the mitochondria were also preserved, while the tonofilaments were reduced in number with abnomal

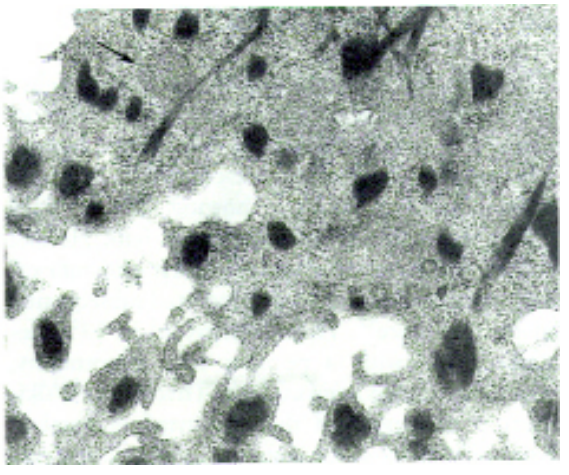

Fig. 6. Round or oval intracytoplasmic dense bodies (arrow) formed by a amorphous finely granular substance in upper spionous cell, measuring 0.5 to 2 ㎛ or more in diameter(EM, ×20,000).

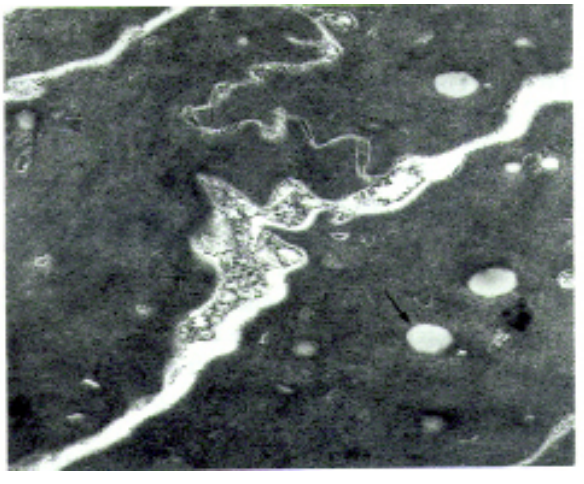

Fig. 7. Numerous round or oval lipoid granules(arrow) in the horny layer(EM, ×20,000).

clumping at the periphery of the cytoplasmic membrane. In the horny layer, a number of round or oval lipoid granules were found(Fig.7).

We treated him with oral antihistamine and topical medications including lactic acid, steroid lotion and keratolytics. After 4 months of treatment, the lesion cleared leaving residual erythema and scale on both proximal extremities. However the lesions were reexacerbated in the following month.

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## DISCUSSION

In 1949, the italian dermatologist Còmel[7] delineated a new type of congenital ichthyosis, which occurred in a 23-year-old woman who suffered from an ichthyosis-like dermatosis characterized by migratory serpiginous skin lesions showing double-edged scaling borders with grossly normal hair. He first coined the term "ichthyosis linearis circumflexa" and sporadic cases have been reported subsequently in the literature[5,9]. Then Netherton[3] in 1958 described ILC with a peculiar hair abnormality, which he termed bamboo hair. Thereafter, Wilkinson et al[4] suggested that the triad of bamboo hair(trichorrhexsis invaginata), ichthyosiform erythroderma and atopic diathesis which usually occurs in common be called Netherton's syndrome(NS). Since that report numerous authors have recognized that most patients ,if not all, with ND have ILC[1,5,6]. In 1974, Mavorah and Frenk[6] suggested that the two disease, ILC and NS, should be considered as close variations of the same disease process. They proposed that statistical analysis in ILC with and without hair change showed significant differences with regard to incidence of scalp involvement, facial lesions and atopic manifestations. Atopic manifestations, which include eosinophilia and increased IgE level as well, are present in many patients and their families, although Traupel doubts whether atopic dermatits is an actual part of the syndrome or not. In our case, we could find no apparent hair shaft abnomalities on repeated microscopic examination of scalp hair, eyebrows, and eyelashs.

Although the heredity of ILC is not yet established clearly , the disease is presumed to be inherited as an autosomal recessive trait with variable expressivity[4,9,10]. ILC is thought to be a relatively rare ichthyosis showing no sexual prevalence. Some patients have seasonal variation. The lesion often improve in summer. Onset occurs at birth or during the first year of life. Many studies have been performed on the morphological and biochemical aspect to clarify the etiology and pathogenesis of this disease[4,11,12,13]. Some abnomal laboratory findings may be seen including intermittent amminoaciduria, eosinophilia, hypogammaglobulinemia, hypergammaglobulinemia, hyperimmunoglobulin E, and low serum Vitamin A level. Aminoaciduria is inconstant and may be due to the influence of long term corticosteroid therapy, which induces adrenal-pituitary axis dysfuction that affects cortisol metabolism and distal renal tubular absorption[2]. Laboratory data of our patient showed mild aminoaciduria. However, we feel that it may not be charcteristic finding for our patient because he had neither a history of recieving corticosteroid therapy nor any renal diseases.

Histologic reports of ILC are not uniform or concordant, and they retain undoubted individuality, but in general, ILC shows an acanthotic epidermis with elongated rete rige ,and a granular layer may be increased or even absent. The horny layer shows hyperkeratosis and focal parakeratosis. In the papillary dermis, perivascular infiltration with mainly lymphohistiocytes and neutrophil can be seen. Some authors described the presence of intraepidermal vesicopustules containing neutrophil[11,12,13]. These findings, Altman et al[5] proposed as 'psoriasis ichthyosis', whereas Stankler et al[14] described only 'eczematous reaction'. Frenk and Mevorah[15] described the presence of round-oval dense bodies containing a finely granular material in the cytoplasm of the prickle cells and also found a decrease of desmosome-tonofilaments complex with a complete absence of keratohyalin. The same authors[13] found PAS-positive, diastase-resistant, Sudan black-positive cytoplasmic granules in the spinous cells and mass-coalesced eosinophilic materials, the histochemical properties of glycolipoproteins, at the stratum corneum level. Thus, they made the hypothesis that the keratinization disturbance leading to the formation of this glycolipoprotein material could be a primary defect, and highly specific and diagnostic in ILC. Frichot et al[16] and Prose et al[17] described similar dense bodies in EM in the patients suffering from atopic dermatitis, and suggested that these structures were lysosomes. Now, it is thought that dense bodies in spinous cells and PAS-posivive granules, which also can be seen in psoriasis[18] or other dermatitis, are not absolutely characteristic but give an unmistakable picture of ILC. Other investigators[12] showed additional findings which are widened extacellular space and dissociated basal cell layer due to amorphous material just above the dilatated upper dermal capillaries. Therefore they stressed the role of dermal infiltration as a primary event of the disease process. On the other hand, Yoshiike[11] et al revealed that ILC has similarities to psoriasis

such as; 1) effectiveness of PUVA therapy, 2)psoriatic change on light and electron microscopy 3) high urinary polyamine level 4) elevated serum enzyme activity in scales and 5) a remarkable change in the keratin molecule which was found to have a small amount of high molecular subunits as well as an increasing number of low molecular ones. They concluded that these may indicate a hyperproliferative situation with a reduced epidermal transit time.

The diagnosis depends on a history of early onset and chronicity ,and the presence of characteristic migratory policyclic lesions with a double-edged scaling border. Early in the course of the disease, it may often be misdiagnosed as Leiner's disease, acrodermatits enteropathica or ichthyosiform erythroderma[5,2,8]. On occasion, ILC can be confused with erythrokeratodermia variabilis[19] but it can be easily differentiated by age of onset, inheritance pattern, area of involvement, clinical course, and histologic features.

With rare exceptions, treatment is not successful. Most patients have been managed with nonspecific treatment including topical corticosteroid, emollients, keratolytic agents, and antibiotics, but withdrawal of these managements allowed a rapid return of the lesion. Nagata et al[20] tried PUVA therapy and reported a good response to the treatment but this required maintenance photochemotherapy. Otherwise, as a therapeutic alteration Vitamine A and retinoids can be used, but in general the result is disappointing[2,6]. Marked progressive and persistent improvement has been observed following oral administration of low dose antimitotic agents to adult patients[21].

We treated our patient with various topical medications of lactic acid, corticosteroid ointment, keratolytics and some emollients. In the course of treatment, it seemed to improve initially, but the lesions were aggravated during continued treatment.

## REFERENCES


1. Traupe H : The ichthyosis. Berlin, Heidelberg: Springer-Verlag,1989.
2. Greene SL, Muller SA : Netherton's syndrome: Report of a case and review of the literature. J Am Acad Derm 13:329-337,1985.
3. Netherton EW : A unique case of trichorrhexis nodosa:" bamboo hair". Arch Dermatol 78:483-487,1958.
4. Wilkinson RD, Curtis GH, Hawk WA : Netherton's disease: trichorrhexis invaginata (bamboo hair), congenital ichthyosiform erythroderma and atopic diathesis; a histopathologic study. Arch Dermatol 89:46-52, 1964.
5. Altman J, Stroud J : Netherton's syndrome and ichthyosis linearis circumflexa:Posiasiform ichthyosis. Arch Dermatol 100:550-558,1969.
6. Mevorah B, Frenk E : Ichthyosis linealis circumflexa Comel : A Clinico-Statistical Approach to its relationship with Netherton's Syndrome . Dermatologica 149:201-209,1974.
7. Comel M : Ichthyosis linearis circumflexa. Dermatologica 98: 133-136, 1949.
8. Hurwitz S, Kirsch N, McGuire J : Reevaluation of ichthyosis and hair shaft abnomalities. Arch Dermol 103:266-271,1971.
9. Stevanovic DV, Pavic RL : Dyskeratosis Ichthyosiformis Congenita migrans: A Variant of Congenital Ichthyosiform Erythroderma. Arch Dermol 78:625-629,1958.
10. Porter PS, Starke JC : Netherton's syndrome. Arch Dis Child 43:319-322,1968.
11. Toshiike T, Manabe M, Negi M, Ogawa H : Ichthyosis linearis circumflexa : morphological and biochemical studies. Br J Dermatol 112,277-283, 1985.
12. Zina AM, Bundino S: Ichthyosis linearis circumflexa Comel and Netherton's syndrome: An Ultrastructural Study. Dermatologica 158:404-412,1979.
13 Mevorah B, Frenk E: Ichthyosis linearis circumflexa with trichorrhexis invaginata ( Netherton's syndrome): A light microscipical study of the skin changes. Dermatologica 149: 193-200,1974.
14. Stankler, L, Cochrane T: Netherton's disease in two sisters. Br J Dermol 79: 187-196,1967.
15. Frenk E, Mevorah B : Ichthyosis linearis circumflexa Comel with trichorrhexis invaginata( Netherton's syndrome).An ultrastructural study of the skin changes. Arch Dermol 245:42-49,1972.
16. Frichot BC, Zelickson AS : Steroid, lysosomes and dermatitis: An ultrastructural study. Acta Derm Venereol 52:311-319,1972.
17. Prose PH, Sedlis E, Bigelow H : The demonstration of lysosomes in the diseased skin of infants with infantile eczema. J Invest Dermatol 45:448-457,1965.
18. Brody I : Light and electron microscopy of excoriated psoriatic lesions in patients during topical treat-

ment. J Cutan Pathol 4:68-79,1977.
19. Brown J, Kierland RR : Erythrokeratodermia variabilis. Arch Dermol 100:550-558,1969
20. Nagata T : Netherton's syndrome which responded to photochemotherapy. Dermatologica 161:51-56, 1980.
21. Klein E, Hahn EM, Solomon JA, et al : Explorations of antimitotic agents in the treatment of a congenital disease :Ichthyosis Linearis Cicumflexa. J Surg Oncol 11:85-88,1979.