A Case of Congenital Ichthyosiform Erythroderma

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Congenital ichthyosiform erythroderma (CIE) is a major type of autosomal recessive congenital ichthyosis showing generalized severe scaling and erythroderma without blistering formation. An affected child is frequently born as a collodion baby. After shedding of the collodion membrane, erythroderma and scaling appear. In classical phenotype of CIE, the entire body is covered in erythrodermic skin with fine white scales. And ectropion and eclabium are frequently seen as well as hyperkeratotic palms and soles. We experienced a 16-year-old male patient who had erythrodermic skin covered with white scales sparing flexural fossa, mild ectropion, palmoplantar hyperkeratosis, and slight contracture of hands. He did not have any other specific personal or family history. Histology of the skin biopsy showed hyperkeratosis with parakeratosis, hypergranulosis, and regular acanthosis in the epidermis. There was mild perivascular cellular infiltration in the upper dermis. These changes are compatible with CIE. (Ann Dermatol 16(4) 197~200, 2004)

Key Words: Autosomal recessive ichthyosis, Congenital ichthyosiform erythroderma

Congenital ichthyosiform erythroderma (CIE) is one of the major types of autosomal recessive severe ichthyosis present at birth[1,2]. This disease is characterized clinically by generallized erythroderma covered with fine, white scales, and is usually manifested as collodion baby at birth[1,2]. In the severe form of this ichthyosis, ectropion and eclabium are present[1,2]. The distinctive histologic changes are mild thickening of the stratum corneum with foci of parakeratosis[2]. We report the case of a patient with a typical presentation of CIE.

CASE REPORT

A 16-year-old boy presented with erythrodermic skin with fine white scales on the whole body, and palmoplantar hyperkeratosis. It had lasted since birth. He was born as a collodion baby. There was no family history of congenital ichthyosis.

On physical examination, he showed a mild ectropion of both eyes and his face showed a waxy appearance. There was the erythroderma with fine white scales on the entire body surface and the scales were larger and darker on the lower legs. His palms and soles showed slight hyperkeratosis and digital contracture was evident on his hands, the finger skin was taut, but the full range of motion was present (Fig. 1). No hypoplasia of nasal, auricular cartilage and scarring alopecia was seen. His hair, nails, and teeth appeared normal. Also his hearing was normal and extracutaneous symptoms were not found.

Histology of a skin biopsy showed slight acanthosis, a moderately thickened horny layer and parakeratosis. The granular layer was prominent. There was a mild perivascular inflammation in the upper dermis (Fig. 2).

On the basis of clinical and histopathologic findings, we diagnosed this case as congenital ichthyosiform erythroderma.

He was treated with a topical corticosteroid and acitretin 20mg daily for 8 weeks. The skin became smoother and the scales were slightly reduced and thinner with this therapy, therefore the acitretin was maintained at a reduced dose of 10 mg daily.

Received July 14, 2004
Accepted for publication September 16, 2004
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Annals of Dermatology
Vol. 16, No. 4, October 2004

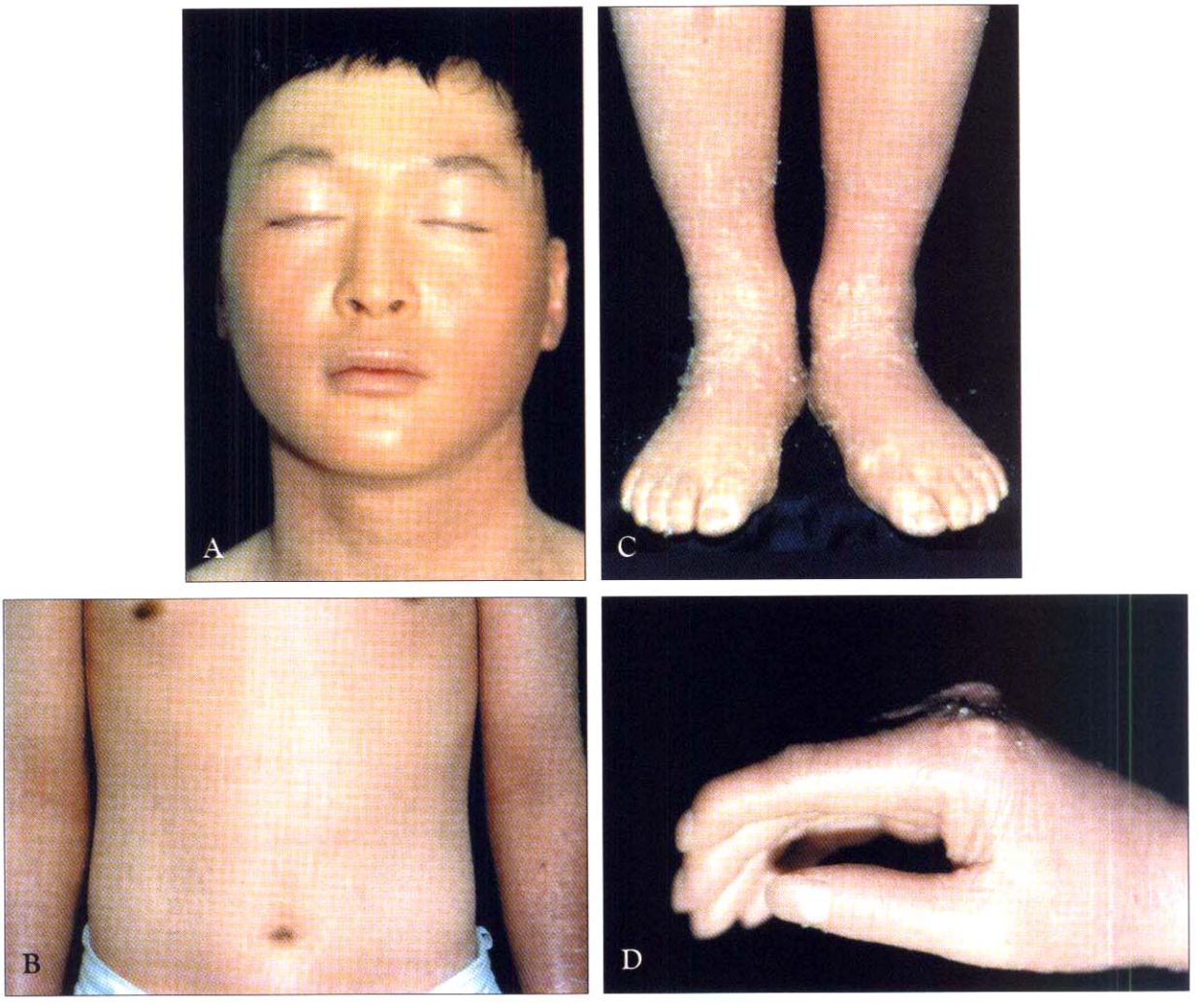

Fig. 1. Clinical appearances of CIE. A mild ectropion of both eyes so the lower eye lids are slightly everted and his face shows a waxy appearance (A), the erythroderma with fine white scales on the trunk and arms (B), lesions on the legs and feet (C) and digital contracture on the hand (D).

DISCUSSION

Autosomal recessive congenital ichthyosis (ARCI) is divided on clinical, histological and molecular genetic grounds into two clinical entities, lamellar ichthyosis (LI) and congenital ichthyosiform erythroderma (CIE)[1]. Until the 1980s, the term LI was used for all nonbullous ARCI and to date LI is still used as a more comprehensive term that includes LI and CIE[1]. Several cases show a phenotype intermediate of the two classic clinical profiles.

CIE appears to be more common than LI, affecting about 1 in 100,000 people[3]. In the vast majority of families, CIE is inherited as an autosomal recessive trait, although autosomal dominant transmission has occasionally been reported[4].

CIE is usually manifested at birth as a collodion baby and after shedding of the collodion membrane, it remains as intense, bright erythroderma with generalized fine white scales[1,2]. Scales may become larger, darker, or plate-like, especially on the extensor surface of the lower extremities[5]. The palms and soles are usually severely affected with a diffuse, fissuring keratoderma that contrasts with the fine, translucent scale elsewhere on the body. Facial skin is taut and flexural folds are also involved[6]. Scales are small relative to those of LI, which also started as collodion baby[7]. Underlying erythroderma is more

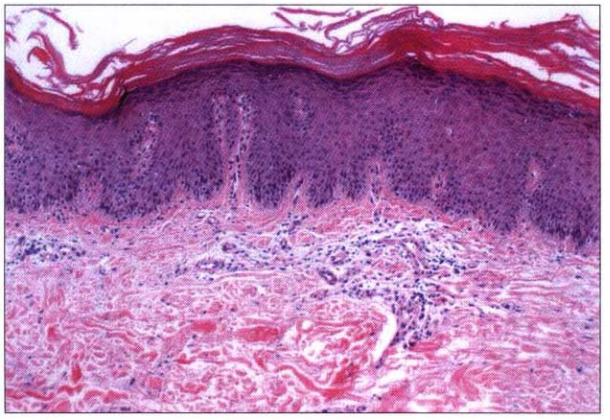

Fig. 2. Moderately thickened horny layer, parakeratosis, slight thickened granular layer, and acanthosis in the epidermis and a mild perivascular inflammation in the upper dermis (H & E, × 100).

visible in CIE, because scales are smaller and thinner than those of LI. In LI, there is minimal to no erythroderma with large, thick, plate like brown scales (Table 1)[7].

There seems to be many variants of CIE ranging from typical patients with collodion membrane, ectropion, eclabium, fine thin scales, flexural involvement, facial tautness and scarring alopecia to less typical cases lacking some or many of these features[6,7]. The hyperkeratosis can interfere with normal sweat gland function, resulting in hypohidrosis that makes the patients have heat intolerance. Secondary nail dystrophy and onychomycosis are not uncommon[6].

The pathomechanisms are known to be heterogeneous and not all the responsible genes have been identified. Only a few patients carry recessive mutations in the keratinocyte transglutaminase-1 (TGM 1) gene located on chromosomal 14q11.2, leading to transglutaminase-1 deficiency[8]. Recently, mutations in the lipoxygenase[3] gene (ALOXE3) or 12-lipoxygenase gene (ALOX12B) located on 17p 13.1 were reported as causative genes[9].

The transglutaminase-1, a membrane-associated transglutaminase of approximately 92kDa, is the largest and major enzyme of the five known transglutaminases expressed in the epidermis, and it plays a key role in the formation of the 10 - 15 nm thick cornified cell envelope. It catalyses calcium-dependent cross-linking of proteins through the formation of Nε-(γ-glutamyl)lysine isodipeptide bonds. The enzyme is expressed in the upper differentiated layers of the epidermis, where it facilitated the formation of the insoluble protein envelopes by cross-linking numerous structural proteins e.g. involucrin, loricrin, small prolin-rich protein, keratin filaments and desmosomal proteins as well as the attachment of the lipid envelope. Hence pathogenic TGM1 mutations seriously perturb the complex process of cornification and desquamation[7,8].

ALOXE3 and ALOX12B encode two closely related enzymes of non-heme, iron-containing dioxygenases. These enzymes catalyze the oxygenation of free and esterified polyunsaturated fatty acids, phospholipids and triglycerides. Thus these are crucial for formation of the epidermal lipid barrier[9].

Histologically, there is focal or extensive parakeratosis and the epidermal acanthosis is more pronounced and accompanied by hypergranulosis. Compared to LI, inflammatory cell infiltration and parakeratosis were seen more frequent in CIE. On the other hand, stratum corneum is usually thicker in LI (Table 1)[7].

Table 1. Comparison CIE with LI

CIE	LI
• Autosomal recessive pattern's inheritance • Born as a collodion baby • Ectropion, Eclabium, Scarring alopecia • Palmoplantar hyperkeratosis	
• Erythroderma with fine, white scales	• Less erythrodermic skin with large, thick, plate-like scales
• Increased epidermal cell turn over rate	• Normal epidermal cell turn over rate
• Parakeratosis and inflammatory cell infiltration in the upper dermis seen more frequent	• Thicker stratum corneum

As topical therapies, hydrating emollients, lubricants, and keratolytics can be used, and the patient requires eye care with liquid tears during the day, and ophthalmic lubricants at night. Disease severity often necessitates systemic therapy with oral retinoids. Acitretin can be very effective in alleviating hyperkeratosis and scaling, but less beneficial in suppressing the erythroderma. It is usually given at lower doses and may be started at 10 to 25 mg/day[10].

To my knowledge, this is the first report in Korean literature, so we report a rare case of a patient present with typical features of CIE.

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