Bullous ichthyosiform erythroderma

Siavash Mohammadzadeh Shanehsaz, MD
Roshan Bittar, MD
Abdollah Anis, MD, PhD
Silva Ishkhanian, MD, PhD

Department of Dermatology and Venereology, Aleppo University Hospital, Syria

Corresponding Author:
Siavash Mohammadzadeh Shanehsaz, MD
Department of Dermatology and Venereology, Aleppo University Hospital, Syria
Email: mdsiavash@yahoo.com

Conflict of interest: none to declare

Received: 10 February 2013
Accepted: 5 June 2013

Bullous ichthyosiform erythroderma (BIE) is a rare disorder of keratinization (mutations in either keratin 1 or 10). It typically presents with fragile skin, which gives way to gradual evolution of hyperkeratosis. Flaccid blisters, peeling, and superficial erosions at sites of minor trauma or friction are apparent within the first few hours of life. Yellow-brown, waxy, ridged or corrugated scales build up in skin creases, sometimes forming spiny (Hystrix) outgrowths. Cobble stone-like keratoses occur at other sites such as the dorsal aspects of the hands and feet and over the trunk. We report an 11-year-old boy with a generalized hyperkeratosis on the neck, trunk, extremities, and scalp.

Keywords: bullous ichthyosiform erythroderma, hystrix, keratinization disorder

Iran J Dermatol 2013; 16: 112-115

INTRODUCTION

Bullous ichthyosiform erythroderma (BIE) is a rare disorder of keratinization. It is also known as epidermolytic hyperkeratosis [1]. BIE is transmitted as an autosomal dominant trait with a prevalence of approximately 1 in 200,000 to 300,000 persons. However, there is a high frequency of spontaneous mutation, and as many as one-half of the cases have no family history and represent new mutation events. Both genders are affected equally [2]. A number of BIE families have been studied and found to have mutations in either keratin 1 or 10 [3]. These keratins are expressed in the differentiated spinous and granular layers of the epidermis, which are the sites of disease pathology in this disorder. KIa I mutations are usually associated with severe palmoplantar keratoderma, whereas KRTlO mutations spare the palms and soles because this gene is not expressed in these locations [4]. Pathogenic mutations leading to non-conservative amino acid substitutions cluster at the boundaries of the a-helical rod region [5]. The characteristic histological features of BIE, hyperkeratosis with lysis and tonofilament clumping in granular layer keratinocytes, are termed epidermolytic hyperkeratosis; in some countries, this term is also used to define the clinical picture of the disease [2]. We report a case of bullous ichthyosiform erythroderma because of its dramatic response to treatment. It is one of the known rare genodermatoses.

CASE REPORT

An 11-year-old boy presented with generalized hyperkeratosis. This complaint started with a generalized erythroderma and flaccid blisters and erosions without scarring at birth. Past medical, family and surgical histories were negative; he was on no medications and he had no history of allergy. Physical examination revealed generalized verrucous hyperkeratosis which covered all of the body except for palms and soles (Figure 1). Yellow-brown scales built up, forming spiny hystrix outgrowths (Figure 2). The central face was mildly affected but scalp involvement was severe and caused patchy alopecia. Skin biopsy shows marked epidermal acanthosis and hyperkeratosis. There are

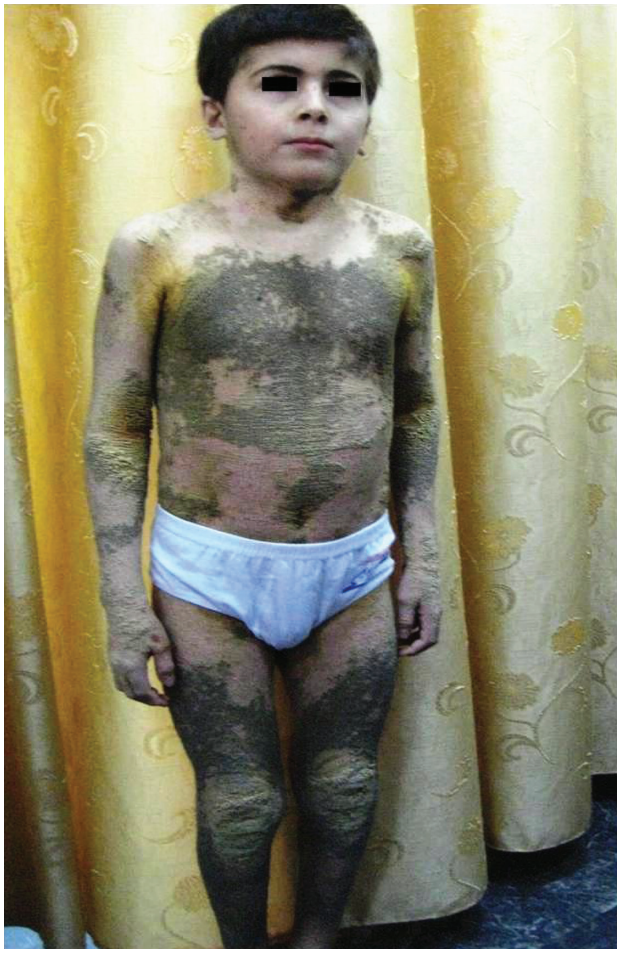

Figure 1. Cobblestone-like keratoses which cover all of the body except for the palms and soles.

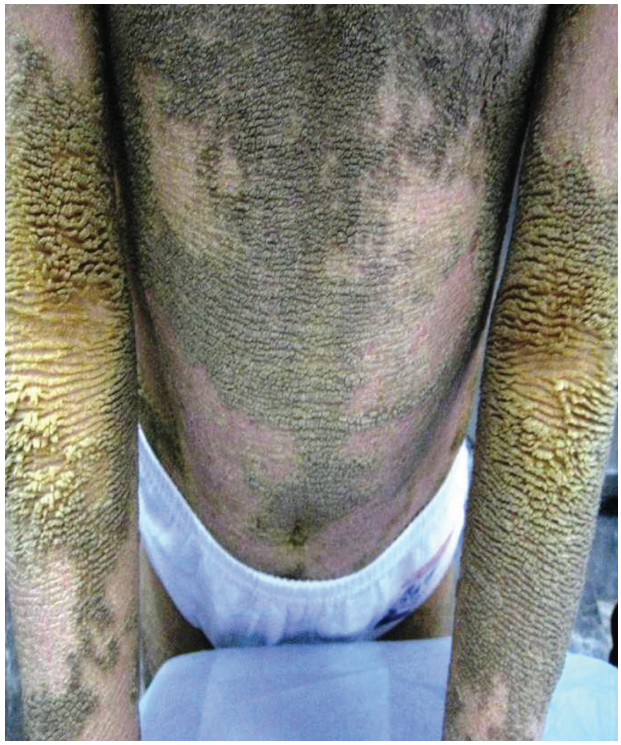

Figure 2. Forming spiny (Hystrix) scales on the flexures.

multiple perinuclear vacuoles and large clumped keratohyalin granules in the cells of the prominent and degenerated granular layer and in the upper spinous layers. Inter and intracellular spaces are formed as a result of suprabasal cytolysis or cell rupture. These features together are described by the term epidermolytic hyperkeratosis (Figure 3). According to these clinical and histopathological data, the diagnosis of BIE was made.

He was treated with acitretin 25mg/day, emollients and urea 10 %. The lesions completely healed about six weeks post treatment without scarring (Figure 4).

DISCUSSION

Bullous ichthyosiform erythroderma typically presents with epidermolysis (fragile skin), which gives way to gradual evolution of hyperkeratosis. A mild generalized erythroderma is present at birth. Flaccid blisters, peeling, and superficial erosions at sites of minor trauma or friction are apparent within the first few hours of life. Yellow-brown, waxy, ridged or corrugated scales build up in skin creases, sometimes forming spiny (hystrix) outgrowths. Cobblestone-like keratoses occur at other sites such as the dorsal aspects of hands and feet and over the trunk [6-10]. BIE is a rare autosomal dominant disorder of keratinization that starts at birth [1]. Frequent misdiagnoses include epidermolysis bullosa, cutaneous mastocytosis, zinc deficiency, staphylococcal scalded skin syndrome, herpetic infection and incontinentia pigmenti. In the past, many of these infants developed severe infection, dehydration, and malnutrition leading to a considerable mortality; therefore, its diagnosis is important. Prenatal diagnosis, based on identification of the characteristic ultrastructural changes on fetal skin biopsy, is traditionally performed at around 20 weeks gestation with ultrasound-guided fetoscopy [11]. Tonofilament clumping is the earliest morphological abnormality which occurs during the second trimester and precedes the formation of keratohyalin granules and stratum corneum [12]. The first trimester prenatal

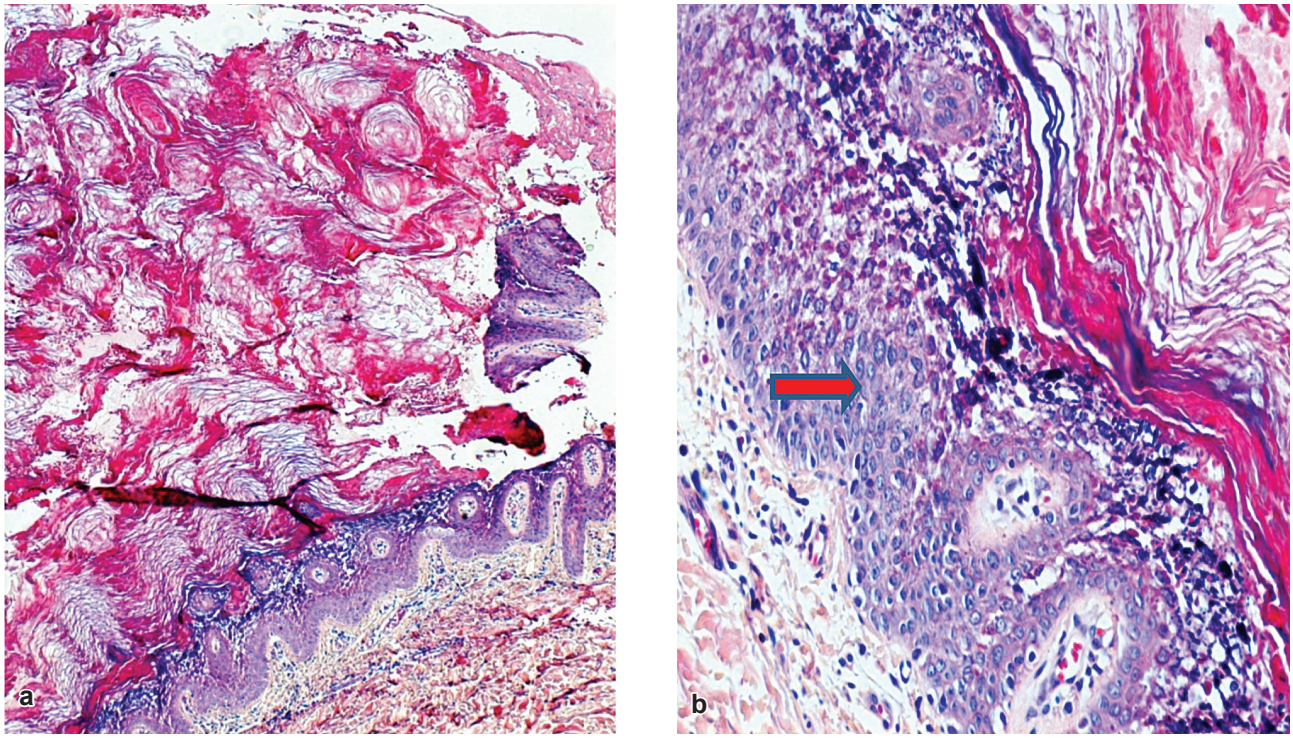

Figure 3. Marked epidermal acanthosis and hyperkeratosiswith multiple perinuclear vacuoles and large clumped keratohyalin granules in the cells of the prominent and degenerated granular layer and in the upper spinous layer (H&E a*20, b*100)

diagnosis is based on DNA screening by direct gene sequencing to identify specific K1 and K10 gene mutations in chorionic villus samples [13,14].

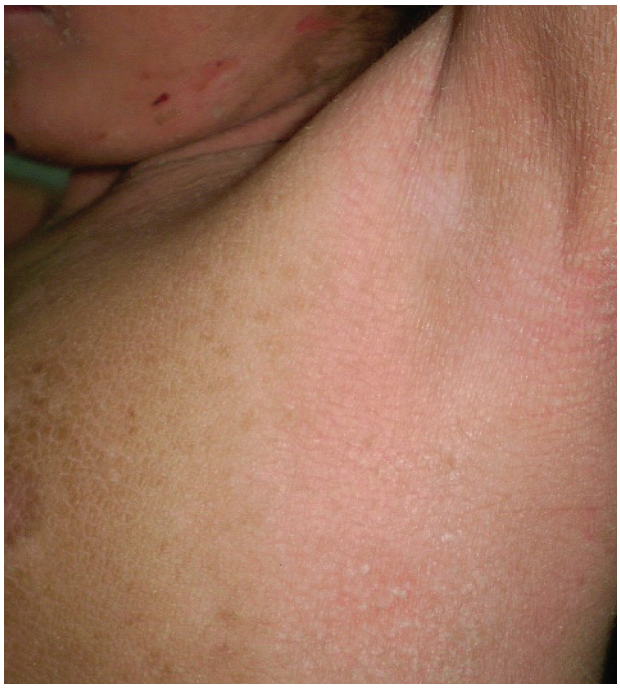

Figure 4. The lesions healed completely six weeks post treatment with acitretin 25mg/day, emollient, and urea 10 % without scarring.

REFERENCES

1. Brocq L. Erythrodermie congenitale ichthyosiforme avec hyperepidermotrophie. Ann Dermatol Syphiligr 1902;4:1-31.
2. Anton-Lamprecht I. Disturbances of tonofilament and keratohyaline structure and arrangement in inborn errors of keratinization. In: Marks R, Christophers E, eds. The Epidermis in Disease, 1st edn. Lancaster: MTP Press, 1981:61-77.
3. Lacz NL, Schwartz RA, Kihiczak G. Epidermolytic hyperkeratosis: a keratin 1 or 10 mutational event. Int J Dermatol 2005;44:1-6.
4. Kwak J, Maverakis E. Epidermolytic hyperkeratosis. Dermatol Online J 2006;12:6.
5. Irvine AD, McLean WH. Human keratin diseases: the increasing spectrum of disease and subtlety of the phenotype-genotype correlation. Br J Dermatol 1999; 140:815-28.
6. Frost P, Van Scott EJ. Ichthyosiform dermatoses: classification based on anatomic and biometric observations. Arch Dermatol 1966; 94: 113-26.
7. Anton-Lamprecht I. Genetically induced abnormalities of epidermal differentiation and ultrastructure in ichthyoses and epidermolyses: pathogenesis, heterogeneity, fetal manifestation and prenatal diagnosis. J Invest Dermatol 1983; 81:149-56.
8. Ross R, DiGiovanna JJ, Capaldi L, et al. Histopathologic characterization of epidermolytic hyperkeratosis: a systematic review of histology from the National Registry for Ichthyosis and Related Skin Disorders. J Am Acad

Dermatol 2008;59:86-90.

9. Mahaisavariya P, Cohen PR, Rapini RP. Incidental epidermolytic hyperkeratosis. Am J Dermatopathol 1995; 17:23-8.
10. Virtanen M, Gedde-Dahl T, Mork NJ, et al. Phenotypic-genotypic correlations in patients with epidermolytic hyperkeratosis and the effects of retinoid therapy on keratin expression. Acta Derm Venereol 2001; 81:163-70.
11. Rothnagel JA, Lin MT, Longley MA, et al. Prenatal diagnosis for keratin mutations to exclude transmission of epidermolytic hyperkeratosis. Prenat Diagn 1998; 18:826-30.
12. Eady RA, Gunner DB, Carbonne LD, et al. Prenatal diagnosis of bullous ichthyosiform erythroderma: detection of tonofilament clumps in fetal epidermis and amniotic fluid cells. J Med Genet 1986; 23:46-51.
13. Rothnagel JA, Longley MA, Holder RA, et al. Prenatal diagnosis of epidermolytic hyperkeratosis by direct gene sequencing. J Invest Dermatol 1994; 102:13-6.
14. Tsuji-Abe Y, Akiyama M, Nakamura H, et al. DNA-based prenatal exclusion of bullous congenital ichthyosiform erythroderma at the early stage, 10–11 weeks of pregnancy in two consequent siblings. J Am Acad Dermatol 2004; 51:1008-11.