Journal of Pakistan Association of Dermatologists 2009; **19**: 168-170.

Case Report

Epidermolytic hyperkeratosis a histological hallmark in the diagnosis of bullous ichthyosiform erythroderma

Asher Ahmed Mashhood, Nadia Iftikhar, Zafar Iqbal Sheikh

Department of Ophthalmology, Military Hospital, Rawalpindi, Pakistan

Abstract

Bullous ichthyosiform erythroderma is an uncommon form childhood keratinizing disorder. Early in life it is associated with generalized blistering and erythroderma. Later on it produces rippled type of hyperkeratosis. The diagnosis is confirmed by a very characteristic histopathology. It is described as "epidermolytic hyperkeratosis". The purpose of this report is to highlight the features of epidermolytic hyperkeratosis and discuss the differential diagnosis of this histological entity.

Key words
Bullous ichthyosiform erythroderma, epidermolytic hyperkeratosis.

Introduction

Epidermolytic hyperkeratosis is a unique histopathological entity characterized by granular degeneration and epidermal cytolysis in upper layers of the epidermis. This entity is typically seen in bullous ichthyosiform erythroderma, but it may be associated with a variety of other diseases, each having a unique clinical appearance.

Case report

Our patient was a 4-year-old girl who was brought to skin outpatient department by her parents with the complaints since birth of generalized dry and thick skin and frequent development of clear fluid filled lesions, which sometimes got infected. According to the parents the girl was born with a normal but slightly dry skin. As she grew old the redness deepened and she developed recurrent flaccid blisters over chest, trunk, forearms and back of legs. Blisters were still erupting, but in addition to a generalized dry skin she was also developing thick and pigmented lesions on dorsum of hands, forearms, feet and legs.

On examination, the patient was a healthy looking young girl with normal milestones. She was non-toxic and had mild pallor. The general physical and systemic examination was unremarkable. On dermatological examination, the patient had generalized ichthyosis (**Figure 1**) with areas of rippled hyperkeratosis on neck, abdomen, back of hands and feet (**Figure 2**). There were multiple superficial erosions over abdomen (**Figure 3**), forearms and ankles. Based on the history and clinical examination the diagnosis of congenital bullous ichthyosiform erythroderma was made and for confirmation, skin biopsy from dorsal surface of right leg was performed. The histopathological appearance was that of massive hyperkeratosis and papillomatosis. There was an intragranular split containing serum and acute inflammatory cell infiltrate and there was a pronounced epidermal hyperplasia (**Figure 4**). The above

Address for correspondence
Lt Col. Asher Ahmed Mashhood,
Assistant Professor of Dermatology,
Military Hospital, Rawalpindi
E-mail: asherahmed67@yahoo.com

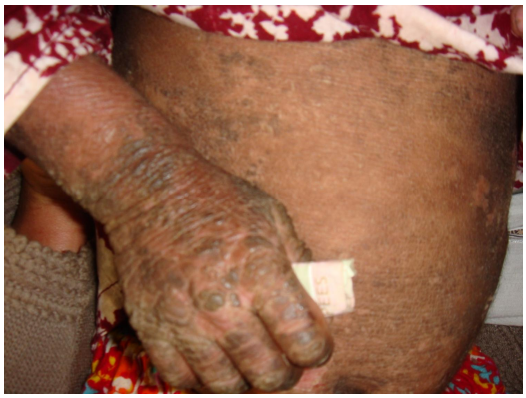

Figure 1 Dry and hyperkeratotic body skin.

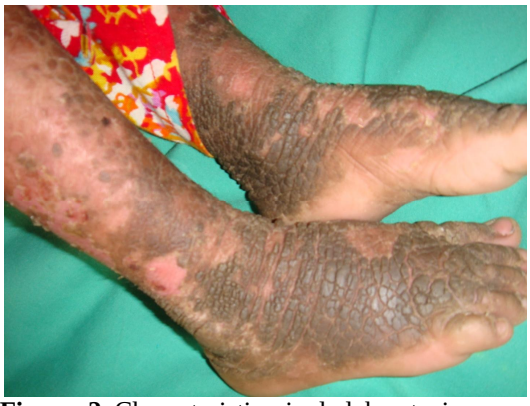

Figure 2 Characteristic rippled keratosis over legs and feet.

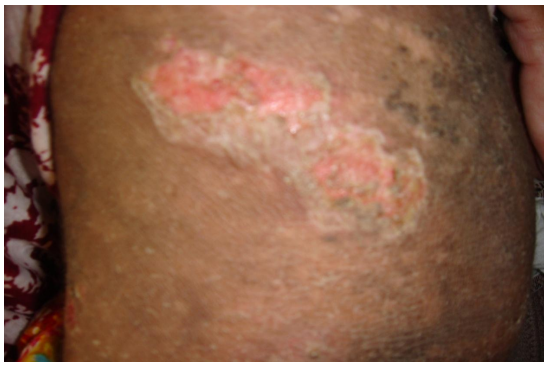

Figure 3 Focal blistering and erosion.

picture was consistent with the characteristic histological appearance of 'epidermolytic hyperkeratosis' seen typically in bullous ichthyosiform erythroderma and a few other diseases.

The patient was advised topical emollients and

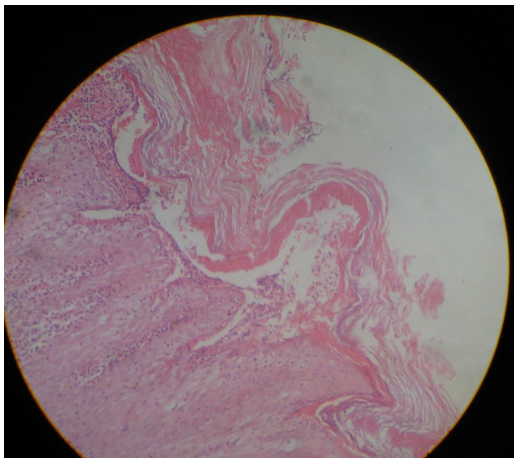

Figure 4 Hyperkeratosis, papillomatosis, intragranular split containing serum, mixed with neutrophils and eosinophils and epidermal hyperplasia.

anti-bacterial ointments for the ulcerated lesions. The parents were explained about the disease and its risk in subsequent pregnancies and were advised regular follow-up in the OPD.

Discussion

Congenital bullous ichthyosiform erythroderma (CBIE) is a very rare disease (incidence 1:300000 births), and although sometimes inherited by an autosomal dominant mode, it more often appears to arise by spontaneous mutation. At birth the infant may show marked hyperkeratosis, erythroderma or even present as a collodion baby. The scales are soon lost, leaving a generalized moist, tender erythroderma followed by development of widespread blistering which heals without scarring. As the patient becomes older, erythema and blistering becomes less apparent and later the disease is complicated by the development of verrucous hyperkeratosis, especially in the flexures. The scales are said to have a quill-like (spiny) appearance (ichthyosis hystrix). In approximately 60% of patients, palmoplantar hyperkeratosis develops with BIE and may result in recurrent painful fissures, contractures

and sclerodactyly. It is however, not related to the disease severity. Nail dystrophy may be a feature. Some cases are complicated by sepsis, fluid loss and electrolyte imbalance.[1] Severely affected children may be of short stature, although many catch up in adolescence.

The condition is associated with markedly increased epidermopoiesis.[2] There is considerable evidence in recent literature, confirming that CBIE represents a genetic disorder of keratin expression[3] with autosomal dominant inheritance. It shows linkage to type II keratin gene cluster on chromosome 12q[4] and 17q. Direct sequencing of keratin 1 and 10 genes has identified point mutations in number of affected families.[5] Interestingly keratin 1 mutation is associated with severe palmoplantar hyperkeratosis while keratin 10 mutations are not.[6]

The histopathological features known as epidermolytic hyperkeratosis (EH) or granular degeneration are very striking.[7] Most characteristically it is associated with, (1) massive hyperkeratosis, papillomatosis and acanthosis, (2) greatly thickened and abnormal granular cell layer, (3) intensely eosinophilic intracytoplasmic inclusions in granular layer, (4) intragranular split due to extreme intracellular edema (cytolysis), and (5) intraepidermal blister formation (following cytolysis). In addition to bullous ichthyosiform erythroderma, there are a few diseases which are associated with this histology. These include ichthyosis bullosa of Siemens, some cases of ichthyosis hystrix, Vorner's palmoplantar keratoderma, a subgroup of linear verrucous epidermal nevi, and epidermolytic acanthoma. It may be an incidental finding in seborrheic keratosis, actinic keratosis, *in situ* squamous cell carcinoma, invasive squamous cell carcinoma, nevi, epidermal and pilar cysts.[8] In such incidental lesions, the changes are limited to one or two dermal papillae in contrast to more extensive involvement in other diseases.

The patients are managed conservatively with the use of topical emollients, appropriate antibiotics and antiseptic creams when required, Topical calcipitriol helps in some cases but may induce irritation. Oral retinoids may be required in severe cases. It reduces scaling but may induce skin fragility and blistering.[9]

References

1. Shwayder T. All about ichthyosis. *Pediatr Clin North* 1991; **38**: 835-57.
2. Frost P, Weinstein GD, Van Scott EJ. The ichthyosiform dermatoses II. Autoradiographic studies of epidermal proliferation. *J Invest Dermatol* 1996; **47**: 561-7.
3. Fuchs E. Genetic Skin disorders of keratin. *J Invest Dermatol* 1992; **99**: 671-4.
4. Comton JG, Digiovanna JJ, Santucci SK. Linkage of epidermolytic hyperkeratosis to the type II keratin gene cluster on chromosome 12q. *Nat Genet* 1992; **1**: 301-5.
5. Rothnagel JA, Dominey AM, Dempsey MD. Mutations in the rod domains of keratins 1 and 10 in epidermolytic hyperkeratosis. *Science* 1992; **257**: 1128-30.
6. DiCiovanna JJ, Bale SJ. Clinical heterogeneity in epidermolytic hyperkeratosis. *Arch Dermatol* 1994; **130**: 1026-35.
7. Holbrook KA, Dale BA, Sybert VP. Epidermolytic hyperkeratosis: ultra structure and biochemistry of skin and amniotic fluid cells from two affected fetus and new born infants. *J Invest Dermatol* 1983; **80**; 222-7.
8. Ackerman AB. Histopathological concepts of epidermolytic hyperkeratosis. *Arch Dermatol* 1970; **102**: 253-59.
9. Blanchet-Bardon C, Nazarro V, Rognin C *et al*. Acitretin in the treatment of severe disorders of keratinization. *J Am Acad Dermatol* 1991; **24**: 982-6.