Bullous Congenital Ichthyosiform Erythroderma and Differential Diagnosis of Widespread Blistering in a Newborn

By Mosunmola Babade, MS, Eliot Mostow, MD, MPH, Robert Brodell, MD

Bullous Congenital Ichthyosiform Erythroderma (BCIE), also termed Epidermolytic Hyperkeratosis, is a rare autosomal dominant disorder that can occur as a spontaneous mutation in 50 percent of cases.1,3 The defect is found in the genes for keratin 1 and Keratin 10.1,2,3 In the US, the frequency is one per 200,000-300,000 persons.2,3 Mortality can result when complications such as sepsis or electrolyte imbalance are not treated aggressively in the neonate period. There is no racial or sex predilection.

Clinically, BCIE is a lifelong condition with onset at birth or in the neonatal period. It presents with erythema, blistering, and/or peeling. Eruptions may be generalized or localized to flexural areas, the face, neck and backs of the hands and feet. In affected areas, the skin is grossly thickened and hyperkeratotic, with deep ridging. Normal skin appearing in the middle of a hyperkeratotic area is a valuable diagnostic sign.1,2,3

Case Report
A 14-hour-old Caucasian boy was born by full term normal spontaneous vaginal delivery. APGAR scores were 9 and 9. Physical examination revealed a well-appearing, afebrile infant with diffuse erythema, widespread bullae, and focal erosions. There was no family history of BCIE. Laboratory tests of the blister fluid were negative for HSV by direct fluorescent antibody. Cultures of stool, urine, and skin were negative for viruses or bacteria. Cerebrospinal fluid analysis was normal; complete blood count revealed normal eosinophil and basophil counts.

Skin biopsy of a vesicle was done with the specimen divided for routine histology and direct immunofluorescence. Hematoxylin and eosin sections revealed a normal dermis and an intact basement membrane and basal layer. Epidermal cells in the granular layer were ballooned and showed prominent marginal keratohyaline granules and overlying keratotic scale typical of epidermolytic hyperkeratosis. Direct immunofluorescence was negative. Findings on electron microscopy revealed normal type IV collagen, laminin, type VII collagen with normal amounts of keratin 5 and 8. There was no evidence of clefts or vesicles at the sub-basilar layer, in the basement membrane, and in the basal layer.

Discussion
BCIE is an incurable, disfiguring condition which has a tremendous impact on family and social life. The disorder is accompanied by a distinct, pungent body odor and is occasionally associated with skeletal, neurological, and ophthalmological abnormalities. Severe scalp involvement leading to encasement, hair loss, and perleche are additional associated findings.1,3

Diagnosis of BCIE is made based on clinical features, histopathological changes, direct immunofluorescence, electron microscopy, and a consideration of inheritance patterns. The differential diagnosis includes Netherton’s syndrome, Icythosiform erythroderma, Conradi syndrome, Ulcereated toxic shock syndrome, Rud’s syndrome, Acute mastocytosis, Staphylococcal Scalded Skin Syndrome, neonatal Herpes simplex, Epidermolysis bullosa, and Second degree burn (See table, above).

Routine H & E histopathology easily identifies the epidermolytic hyperkeratosis typical of BCIE and distinguishes most of the other conditions. A negative direct immunofluorescence

Continued on p. 58

Differential Diagnosis of Widespread Erythroderma and Blistering in a Newborn

- Netherton’s syndrome
- Ichthyosiform erythroderma
- Conradi’s syndrome
- Ulcereated toxic shock syndrome
- Rud’s syndrome
- Acute mastocytosis
- Staphylococcal Scalded Skin Syndrome
- Neonatal Herpes simplex
- Epidermolysis bullosa
- Second degree burn
New In Your Practice

Deficiency Report. Eczema herpeticum occurs in some patients with atopic dermatitis due to disseminated infection with herpes simplex virus (HSV), but why some patients develop the disease is unclear. Perhaps deficiency of cathelicidin, an antimicrobial peptide, raises susceptibility to eczema herpeticum, according to results of a recent study in the Journal of Allergy and Clinical Immunology (2006; 117: 836-841). Researchers assessed cathelicidin activity in vitro and in mice, and, additional, cathelicidin levels were measured in skin biopsy specimens from 10 AD patients without HSV and from 10 with eczema herpeticum. Skin expression of cathelicidin was lower in the subjects with eczema herpeticum than in those with HSV skin infection.

Futile PET? In detecting occult melanoma metastases, early positron emission tomography (PET) is of a little help for melanoma patients with clinical stage I or II disease, a new study finds (Archives of Surgery, 2006; 141: 284-288). Researchers retrospectively studied data of 64 patients with T2 to T4 melanomas who had undergone PET as part of their preoperative evaluation. The PET did not find any occult distant metastases, leading researchers to conclude that PET did not change clinical management in any of the patients.

Continued from p. 60

study excludes the diagnosis of acquired epidermolysis bullosa. Electron microscopy differentiates BCIE from various forms of inherited scarring and non-scarring epidermolysis bullosa. The direct fluorescent antibody test of a smear specimen taken from the base and roof of a blister is the quickest way to identify multinucleated giant cells of Herpes simplex infections. The correct diagnosis is essential for appropriate management of this serious disorder and for genetic counseling.

BCIE could be a potentially life threatening condition. Therapy is symptomatic and should be adapted to the age of the patient. It is primarily aimed at reducing hyperkeratosis. In the neonatal period, patients require management in an intensive care nursery to provide protective isolation and to prevent dehydration, electrolyte imbalance, hyperpyrexia and cutaneous superinfection.

When neonates are handled carefully with protective padding and lubricants used, erosions and denuded skin usually cornify rapidly. Keratolytic agents containing urea, salicylic acid and alpha hydroxyl acids, as well as topical tretinoin and vitamin D preparations are effective but are sometimes irritating. Benefits and side effects must be carefully considered, since long term therapy is usually required. Frequent follow-up is required to immediately treat secondary bacterial infections.