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Nonbullous Congenital Ichthyosiform Erythroderma in a Neonate

Fu-Min Wang, Chih-Chien Wang, Chuen-Ming Le, and Wen-Tsung Lo*

Department of Pediatrics, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan, Republic of China.

Nonbullous congenital ichthyosiform erythroderma (NBCIE) in newborns usually presents with a transparent covering that desquamates over 10 to 14 days. We describe a patient admitted to our intensive care unit with a generalized exfoliative erythroderma and clinical signs and biopsy specimen findings consistent with NBCIE. The patient was born as a collodion baby and has remarkably improved after antibiotic treatment and application of topical emollients without severe side effects.

Keywords: Nonbullous congenital ichthyosiform erythroderma, staphylococcal scalded skin syndrome, lamellar ichthyosis

INTRODUCTION

Neonatal nonbullous congenital ichthyosiform erythroderma (NBCIE) is an autosomal recessive form of inherited ichthyosis. The incidence of this disorder is about 1 in 300,000 births. Clinically, NBCIE appears as generalized erythroderma with fine white scales that gradually replace the collodion membrane. Other associations include ectropion, eclabium, scalp alopecia, decreased sweating with heat intolerance, and nail dystrophy. Treatment is based on the severity of the disease. Topical treatments including emollients, keratolytics, lactic acid, and propylene glycol are effective, but their application is limited because of their adverse effect of local irritation. Systemic use of retinoid is also applicable for the treatment of severe NBCIE. We describe a premature male newborn who developed NBCIE with methicillin-resistant Staphylococcus infection, and discuss relevant pathology and issues in clinical management.

CASE REPORT

A male neonate, weighing 2365 g, was born at GA 36 5/7 weeks by cesarean section because of preterm premature rupture of membranes. The Apgar score was 7 and 9 at one and five minutes, respectively. The mother, who works in the surgical intensive care unit of our hospital, was healthy and had no family history of any hereditary skin disease. Adequate antibiotic coverage was given to the mother before delivery. After delivery, the baby was noted to have a cling-film-like membrane all over his skin. The typical features of collodion baby were noted. After birth, generalized erythroderma with some epidermal peeling over the face, trunk and the four limbs was noticed (Figure 1), and hypothermia (35.7 ^{o}C), tachypnea (pulse 170 beats/min), respiratory retraction and frequent desaturation (SPO_2 70-80%) were found with suspicions of neonatal sepsis. The Nikolsky sign was positive. The mucous membranes of the mouth and anus were unaffected and hair was sparse. There was no ectropion or eclabium.

Pinnae and nasal passages were normal. No constriction bands or blisters were noted. Laboratory tests obtained after delivery showed a normal blood count. Chromosomal studies revealed a male karyotype (46, XY) with no apparent abnormalities. Cultures from the scalded-skin lesion and the bloodstream were obtained at day 1 of life. The culture of the scalded-skin lesion grew methicillin-resistant *Staphylococcus aureus* (MRSA), whereas the bloodstream culture was sterile. The MRSA grown from the skin produced toxic shock syndrome toxin-1 (TSST-1) but was negative for the exfoliative toxins A (ETA) and B (ETB). A skin biopsy performed at day 10 of life showed no splitting at the granular layer of the epidermis and no inflammatory infiltrates, with mild thickening of the orthokeratotic cornified layer and no epidermolytic hyperkeratosis. The granular cell layer was slightly increased. There were no cholesterol crystals found (Figure 2).

Treatment included administration of intravenous antibiotics and fluids. Infection control measures were immediately implemented and included isolation of the infected

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*Corresponding author: Wen-Tsung Lo, Department of Pediatrics, Tri-Service General Hospital, National Defense Medical Center, No. 325, Sec.2, Cheng-Gong Rd, Taipei 114, Taiwan, Republic of China. Tel: +886-2-87927025; FAX: +886-2-87927293; E-mail: drluoped@yahoo.com.tw

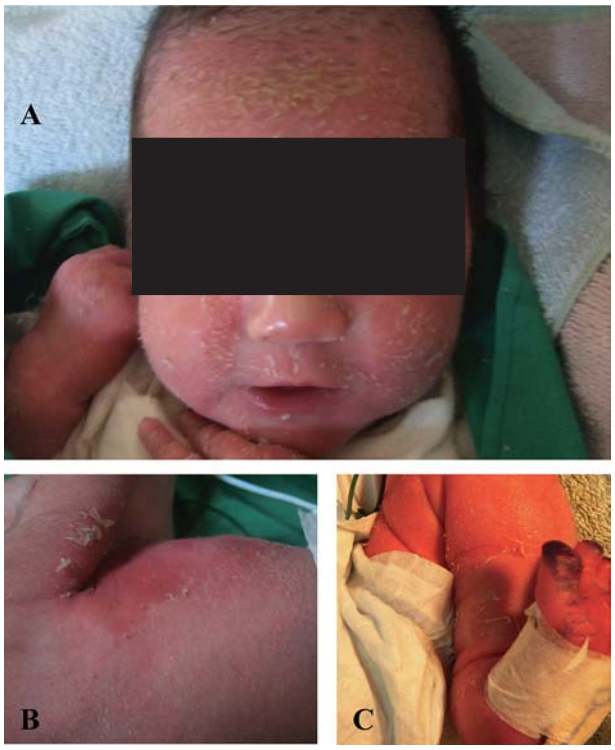

Fig. 1 Clinical photograph showing the extensive areas of peeling skin characteristic of nonbullous congenital ichthyosiform erythroderma. A.face, B.axillary, C. leg .

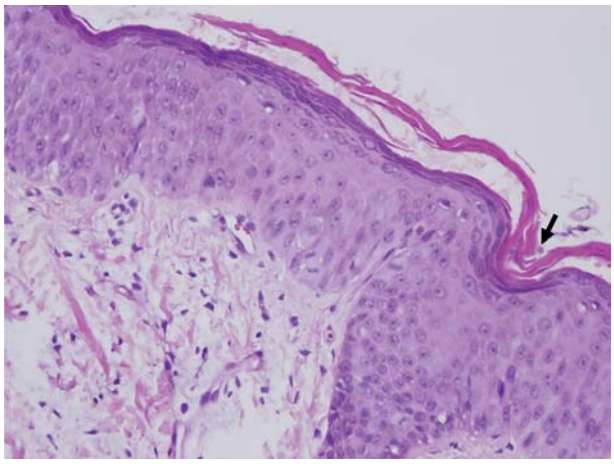

Fig. 2 Histologic examination of a skin biopsy specimen from the left leg lesion shows mild thickening of the orthokeratotic cornified layer with no epidermolytic hyperkeratosis (*arrows*). No characteristic splitting at the granular layer of the epidermis and no inflammatory infiltrates were found. The granular cell layer is normal and no cholesterol crystals were found. (Hematoxylin ― eosin stain; original magnification × 200.)

infant. Vancomycin was administered intravenously for 14 days in accordance with the culture sensitivity report. Supportive management included Vaseline application for skin care. Improvement was noted with time as the collodion membrane shed, leaving generalized erythroderma. After the collodion membrane was shed, progressive improvement was noted with frequent emollient applications alone. Resolution was near complete three months later, with only mild residual ichthyosis at the sacral area.

DISCUSSION

Erythroderma is defined as an inflammatory skin disorder affecting more than 90% of the body surface[1]. NBCIE is a rare nonblistering disorder characterized by fine grayish-white scales and erythroderma. The disorder is inherited as an autosomal recessive trait except for a few cases caused by a dominant trait. An affected newborn is frequently born as a collodion baby (covered with oiled parchment-like shiny skin)[2]. Other symptoms include alopecia, deep skin fissures and nail dystrophy but the teeth and mucosal surfaces are normal[3]. Hyperkeratosis is particularly noticeable around the knees, elbows, and ankles. The face is often markedly involved, including ectropion, flattening of the ears and nose, and fixation of the lips in an O-shaped configuration. The disorder is present soon or shortly after birth and is the most common form of ichthyosis to present as a collodion baby with a glistening membrane resembling sausage skin[4]. Our patient was covered at birth in a thick, taut membrane resembling collodion. After shedding this collodion membrane, generalized scaly erythroderma was apparent and persisted for several weeks.

Since the 1980s, nonbullous autosomal recessive ichthyoses have been divided into two major clinical entities, NBCIE and lamellar ichthyosis (LI)[5]. The nature of scaling and intensity of erythroderma are important clinical features that distinguish NBCIE and LI. After shedding of the collodion membrane, generalized erythroderma with fine, white or gray scales, different from the large, dark scales seen in LI, was evident in our patient[6]. In some families with LI, transglutaminase 1 gene mutations have been identified as causative genetic defects, and transglutaminase 1 is thought to be one of the candidate molecules for NBCIE[7].

NBCIE is unlike bullous congenital ichthyosiform erythroderma (BCIE), which is a severe autosomal dominant congenital ichthyosis which exhibits widespread blisters

and erosions in the erythrodermic skin at birth[4]. The entire skin is rarely involved and the scales of epidermolytic hyperkeratosis are thick, gray-brown, and often verrucous in areas of flexion over the knees and elbows. Histologically, predominant vacuolation of the cells is observed in the middle and upper spinous layers and granular layers. The vacuolated keratinocytes have large and irregularly shaped granules. The light microscopic findings are characterized by hyperkeratosis, papillomatosis, acanthosis and vacuolization of the granular and upper prickle cell layers.

In addition, exfoliative skin diseases are rare in neonates. When causation by *S. aureus* is a possibility, scalded-skin diseases such as staphylococcal scalded-skin syndrome (SSSS) may be considered. Differential diagnosis of general erythroderma and infectious disease, SSSS and toxic shock syndrome should be considered. SSSS is caused by the circulation of ETA and ETB produced by staphylococci in focal infections such as conjunctivitis, omphalitis, or rhinitis[8]. Some congenital and neonatal cases (following chorioamnionitis) have been described[9]. Within one to two days, the patients develop a generalized macular and subsequently erythrodermic rash, which is accompanied by increased skin tenderness. Skin biopsy of SSSS reveals a split in the granular layer of the skin, induced proteolysis, and might exhibit evidence of superantigen activities, such as epidermolysis and lymphocyte mitogenicity. This precedes the formation of subcorneal blisters, exudation, crusting, and, finally, generalized exfoliation. In our patient, SSSS is ruled out by negative findings for ETA and ETB in microbial studies and the skin biopsy result. Although TSST-1 was positive, this infant did not fulfill the criteria for toxic shock syndrome[10].

Treatment is symptomatic with a high-humidity environment, and application of nonocclusive lubricants may facilitate shedding of the membrane. Emollients remain the mainstay of treatment. Generous and frequent applications of emollients and keratolytic agents such as lactic or glycolic acid (5%), urea (10-40%), and retinoic acid (0.1% cream) may lessen the scaling to some extent, although these agents produce stinging if applied to fissured skin[11,12]. The long-term risks of these compounds (teratogenic effects and toxicity to bone) may limit their usefulness. Prevention of sunburn and sunstroke is important. Ectropion requires ophthalmologic care, and, at times, plastic procedures.

Neonatal morbidity and deaths may be caused by cutaneous infection, aspiration pneumonia (squamous material), hypothermia, or hypernatremic dehydration from excessive transcutaneous fluid losses resulting from increased skin permeability.

In conclusion, neonatal exfoliative erythroderma is a rare condition and can be potentially life threatening irrespective of the cause, and must be carefully differentiated from ichthyosiform disorders. It is usually difficult to establish a diagnosis of the condition because of the poor specificity of the clinical and histological signs, but certain parameters may be helpful in making the diagnosis. Careful monitoring and management of the patients may improve the outcome.

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