

Staphylococcal Scalded-Skin Syndrome in a Very Low Birth Weight Premature Infant

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ABSTRACT. Exfoliative skin diseases are rare in neonates. When caused by coagulase-positive *Staphylococcus aureus*, scalded-skin diseases such as staphylococcal scalded-skin syndrome (SSSS), bullous impetigo, and staphylococcal scarlet fever may develop. These diseases might cause significant complications and mortality. SSSS is caused by staphylococcal exfoliative toxins A or B, which split the granular layer of the skin, induce proteolysis, and might exhibit superantigen activities, such as epidermolysis and lymphocyte mitogenicity. We describe a 1378-g premature male infant who was born at 29 weeks' gestation and developed SSSS on day 3 of life, with no clinical signs of neonatal sepsis. After cultures from the lesion and bloodstream were obtained, intravenous cloxacillin therapy was started. Infection control measures were implemented instantly and included isolation of the infected infant, personnel handwashing with hexachlorophene, and placement of exposed neonates into a cohort. The initial lesion expanded and additional lesions appeared, but 12 hours after initiation of antibacterial therapy, the lesions ceased to proliferate. Cultures from scalded-skin lesions grew coagulase-positive *Staphylococcus aureus*, whereas the bloodstream culture was sterile. The lesions resolved completely within 6 days, and the infant's subsequent course was uneventful. No similar skin lesions were noticed in other infants in the neonatal intensive care unit. We discuss recent advances in understanding the pathogenesis of neonatal SSSS, highlight the importance of early diagnosis and treatment, and stress the need for new adjunctive therapies for this disease. *Pediatrics* 2001;108(1). URL: <http://www.pediatrics.org/cgi/content/full/108/1/e16>; *premature infant, very low birth weight, Staphylococcus aureus, scalded-skin syndrome*.

ABBREVIATIONS. VLBW, very low birth weight; CPSA, coagulase-positive *Staphylococcus aureus*; NICU, neonatal intensive care unit; ETA, exfoliative toxin A; ETB, exfoliative toxin B; SSSS, staphylococcal scalded-skin syndrome; BI, bullous impetigo.

Exfoliative skin diseases are rare in neonates, especially in very low birth weight (VLBW) infants. When caused by coagulase-positive *Staphylococcus aureus* (CPSA), these diseases might be associated with significant complications and mor-

tality. We describe a VLBW premature infant who developed staphylococcal scalded-skin disease, discuss recent advances in understanding its pathogenesis, highlight the importance of early diagnosis and treatment, and stress the need for new adjunctive therapies.

CASE REPORT

A 1378-g premature male infant was the first of twins, born at 29 weeks' gestation by cesarean section after premature uterine contractions. The Apgar score was 6 and 7 at 1 and 5 minutes, respectively. The mother was healthy and had no family history of hereditary skin disease. Pregnancy was uneventful without premature rupture of membranes. Corticosteroids were given to the mother before delivery. The infant experienced transient tachypnea of newborn. Laboratory tests obtained after delivery showed a normal blood count and no growth of bacteria or fungi in cultures of bloodstream, external ear, or gastric aspirate. Specific IgM titers for toxoplasmosis, cytomegalovirus, rubella, and herpes simplex were negative.

On day 3 of life, an 8 × 7-mm skin lesion with blisters and epidermal peeling was noticed on the right upper thigh with no clinical signs of neonatal sepsis. Nikolsky's sign was positive. Cultures from the lesion and the bloodstream were obtained, and intravenous cloxacillin therapy was started. A skin biopsy was not performed. Infection control measures were implemented instantly and included isolation of the infected infant, personnel handwashing with hexachlorophene, and placement of exposed neonates into a cohort. Skin cultures from members of the neonatal intensive care unit (NICU) medical and nursing staff were not obtained.

Within 3 hours, the initial lesion expanded and a perioral erythematous lesion was noticed. In addition, 2 new rapidly spreading skin lesions on the left upper thigh and on the periumbilical area appeared within 4 and 6 hours, respectively (Fig 1), but 12 hours after initiation of antibacterial therapy, the lesions ceased to expand or proliferate. Cultures obtained from periumbilical and right thigh skin grew CPSA, whereas the bloodstream culture was sterile. Because of technical problems, identification of exfoliative toxins A (ETA) and B (ETB) was not performed. Complete blood counts were normal. Six days later, the lesions had resolved completely and the infant's subsequent course was uneventful. During this period, no similar skin lesions were noticed in the infant's twin or in other infants in the neonatal intensive care unit.

DISCUSSION

The differential diagnosis of the described exfoliative skin lesions in neonates includes staphylococcal scalded-skin syndrome (SSSS), bullous impetigo (BI), drug-induced toxic epidermal necrolysis, epidermolysis bullosa, bullous mastocytosis, herpetic lesions, and neonatal pemphigus. In our VLBW premature infant, the history, the exfoliative nature of the skin lesion, the course of disease, and the growth of CPSA from skin lesions suggest the diagnosis of SSSS or BI.

Three forms of staphylococcal skin disease have been described in neonates: SSSS, BI, and a generalized scarlatiniform eruption without exfoliation

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Fig 1. Skin lesions on the upper thighs with superficial epidermal peeling and a periumbilical skin lesion with exudative erosions, 24 hours after onset of disease.

(staphylococcal scarlet fever).¹ SSSS (Ritter's disease) and BI have many clinical features in common, and the lesions of BI are actually considered to represent a localized form of SSSS. However, compared with BI, the skin lesions of SSSS are larger, CPSA is less frequently isolated, and less inflammatory infiltrate in the skin lesions is noticed.¹ Characteristically, SSSS consists of diffuse erosions, with epidermal separation in the subcorneal layer through the granular layer,² whereas in BI, a flaccid, transparent bulla develops most commonly on the skin of the face, buttocks, trunk, perineum, and extremities and in the diaper area.

SSSS is caused by staphylococcal ETA and ETB, secreted mainly from phage II staphylococci and strains 71, 3A, 3B, 3C, and 55.³ In the absence of specific antibodies against ETA and ETB, as is the case mainly in infants and children, these toxins spread hematogenously and cause SSSS. ETA and ETB differ in that ETA is encoded by bacterial genes and is heat stable, whereas ETB is encoded on a plasmid and is heat labile.² The split in the granular layer is attributable to the binding of ETA or ETB to desmoglein I within desmosomes² and to keratohyalin granules of the granular layer.⁴ These toxins induce proteolysis by trypsin-like serine proteases.^{5,6} Also of note is that the catalytic site of V8 protease is present both in ETA and in ETB.⁷

Recent work suggests that ETA exhibits superantigen activities, such as epidermolysis and lymphocyte mitogenicity, whereas several single amino acid mutants of ETA lack the T-lymphocyte mitogenic activity.^{5,8} All ETA mutants that have lost the esterase activity were found also to have lost the epidermolytic activity, whereas a persistent esterase activity also retained the epidermolytic ability.⁵ Furthermore, incubation of partially purified exfoliative toxin with serine protease inhibitors before inoculation into mice delayed epidermal splitting.⁷ These observations implicate serine protease activity in the causation of SSSS.

In BI, CPSA is always the causative organism and can be isolated from skin lesions but rarely from the bloodstream.⁸ The same exfoliative toxins of SSSS (ETA, ETB) also are found in cases of BI and play a role in the exfoliative process of this localized disease.⁸

SSSS and BI have been reported predominantly in infants and children <5 years, because children in this age group lack specific anti-ETA and anti-ETB antibodies.⁹ ETA antibody was detected in 88% of cord blood samples. This rate diminished to 30% at 3 to 24 months and rose again to 91% by 40 years of age.¹⁰ Septicemia is not a common feature of SSSS in newborn infants. To date, SSSS and BI have been reported in 9 premature infants; only 1 patient's disease was associated with sepsis, and the patient died.^{1,11-16}

Medical staff who are infected or colonized with exfoliative toxin-producing CPSA usually are the source of outbreaks of SSSS and BI in the NICU, and CPSA can be isolated from the anterior nostrils of 25% and 27% of NICU medical and nursing staff, respectively.^{3,13} The complications of SSSS and BI in children and infants include fluid loss, dehydration, cellulitis, pneumonia, sepsis, osteomyelitis, septic arthritis, necrotizing fasciitis, and a 4% risk of mortality.^{2,9,17}

SSSS may be life threatening in VLBW premature infants and can provoke serious outbreaks of the disease in the NICU. A high index of suspicion, prompt diagnosis, implementation of infection control measures, and early institution of treatment all are indispensable steps for halting the expansion of SSSS in the infant, avoiding complications and mortality, and preventing the spread of disease to other infants.

In the neonate described here, the above-mentioned infection control measures were successful in preventing nosocomial spread to the other NICU infants. Despite SSSS/BI in our infant, no systemic signs of sepsis were evident; therefore, additional therapies, such as pooled human immunoglobulins, did not become warranted. Future development of specific anti-ETA and anti-ETB antibodies might enrich our therapeutic arsenal and help in slowing the expansion of SSSS, lessening its severity, and minimizing its complications. Such therapeutic approach becomes particularly important in view of the growing rate of SSSS that is caused by methicillin-resistant CPSA.^{18,19}

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