

Staphylococcal Scalded Skin Syndrome as a Harbinger of Late-onset Staphylococcal Septicaemia in a Premature Infant of Very Low Birth Weight

Matthias Hütten¹, Konrad Heimann¹, Jens M. Baron², Tobias G. Wenzl¹, Hans-Friedrich Merk² and Hagen Ott^{2*}

Departments of ¹Neonatology and Paediatric Intensive Care Medicine, and ²Dermatology and Allergology, University Hospital of the RWTH Aachen, Pauwelsstrasse 30, D-52074 Aachen, Germany. *E-mail: hagen.ott@post.rwth-aachen.de

Accepted January 7, 2008.

Sir,

Blistering skin disorders are rare conditions in neonates and infants presenting with a broad range of differential diagnoses and potentially fatal clinical sequelae. Although rarely encountered, exfoliative toxins synthesized by coagulase-positive Staphylococci must be considered as a possible underlying cause, as they are known to induce staphylococcal scalded skin syndrome (SSSS, Ritter's disease) (1). We report here on a preterm infant who developed SSSS as presenting sign of septicaemia caused by a *Staphylococcus aureus* strain producing exfoliative toxins A and B.

CASE REPORT

A male infant of extremely low birth weight (985 g) born prematurely at 29 weeks of gestation was readmitted to our neonatal intensive care unit at the age of 37 days for sudden-onset bradycardia and intermittent apnoea associated with poor feeding and marked irritability. He had developed exudative skin lesions under the headgear of a respiratory mask employed for continuous positive airway pressure (CPAP) ventilation (Fig. 1). While an erythematous rash or other preceding symptoms were not observed, the infant developed confluent flaccid blisters after minor skin trauma caused by adhesive tapes and sticking electrodes. Nikolski's sign was positive and 15% of his body surface area was

affected by epidermal desquamation, while the mucous membranes were intact and the skin appendages did not show any abnormalities.

Due to the patient's rapidly worsening general condition, a skin biopsy was not performed. However, we immediately initiated intravenous antibiotic therapy with cefuroxime (100 mg/kg body weight) after the microbiological work-up (blood culture, skin and mucosal swabs) had been completed. Infection control measures were implemented promptly and the infant was laid on sterile cloths in an incubator with high air humidity and minimal handling. He received 100% maintenance fluid plus the Parkland correction for a 15% burn to compensate for fluid loss associated with the extensive skin barrier disruption.

Within 24 h, further bullae appeared on the patient's trunk and extremities (Fig. 2), while laboratory examinations revealed leukopaenia ($7.0 \mu\text{l}^{-1}$) and C-reactive protein elevation (44 mg/l). However, on the second day, the blisters ceased to expand and the infant's cardiorespiratory situation improved constantly. The further course was uncomplicated and 7 days later the skin lesions had resolved completely without scarring or post-inflammatory hyperpigmentation.

DISCUSSION

Periumbilical and nose swabs as well as blood culture specimen harboured coagulase-positive *S. aureus* strains that were shown to express exfoliative toxins



Fig. 1. Exudative facial skin lesions due to continuous positive airway pressure mask pressure and bullae on the trunk caused by electrocardiogram (ECG) and transcutaneous O_2/CO_2 -sticking electrodes.



Fig. 2. Eroded bulla of the right palm following peripheral venous line placement.

A and B (ETA and ETB) as determined by PCR (Professor Dr W. Witte, Robert-Koch-Institute, National Reference Centre for Staphylococci, Berlin, Germany), while cultures of blister fluid remained sterile.

The differential diagnosis of neonatal and infantile skin exfoliation comprises hereditary (epidermolysis bullosa, ichthyosis bullosa, bullous mastocytosis), immune-mediated (pemphigus neonatorum, toxic epidermal necrolysis) and infectious (bullous impetigo, SSSS) diseases.

SSSS is caused by the ETA and ETB, which are usually synthesized by phage II *S. aureus* strains. Currently, these epidermotropic toxins are regarded as glutamic acid-specific, trypsin-like serine proteases that are capable of inducing a proteolytic cleavage of the desmosomal protein desmoglein I (2–4). This impairment of cell-cell adhesion leads to intra-epidermal blistering and the clinical picture of exfoliative dermatitis, which is observed mainly in infants and toddlers, but has also been described in rare cases in premature infants (5–8). Interestingly, these age groups are particularly prone to develop exfoliative dermatitis as they show limited renal toxin elimination (3) and display a relative lack of neutralizing toxin-specific antibodies (2, 9). In this context, it remains unknown whether the simultaneous production of both ETA and ETB, that was observed in our patient and is thought to occur in about 50% of affected children (10), contributes to disease severity.

To the best of our knowledge, this is one of only three published cases describing SSSS and staphylococcal septicaemia in premature infants. While the other two neonates developed early-onset sepsis directly postpartum and on day 5 respectively, clinical symptoms of SSSS occurred at the end of our patient's neonatal period and prompted the diagnosis of late-onset staphylococcal septicaemia. This facilitated immediate antibiotic treatment and therefore helped avoid serious and potentially fatal complications of invasive staphylococcal disease. Although a skin biopsy was not performed in our critically ill patient, this diagnostic tool is essential if the clinical picture remains unclear and particularly if

toxic epidermal necrolysis (TEN) is suspected. Whereas TEN is an immune-mediated disease triggered by drugs and/or viral infections that almost always affects one or more mucous membranes, it might resemble SSSS in the prodromal period and can only be distinguished by its characteristic feature of complete epidermal necrosis on histological examination (11).

REFERENCES

1. Ladhani S. Staphylococcal toxins and the scalded skin syndrome. *Br J Dermatol* 2000; 142: 195–196.
2. Ladhani S, Joannou CL, Lochrie DP, Evans RW, Poston SM, et al. Clinical, microbial, and biochemical aspects of the exfoliative toxins causing staphylococcal scalded-skin syndrome. *Clin Microbiol Rev* 1999; 12: 224–242.
3. Hanakawa Y, Schechter NM, Lin C, Garza L, Li H, Yamaguchi T, et al. Molecular mechanisms of blister formation in bullous impetigo and staphylococcal scalded skin syndrome. *J Clin Invest* 2002; 110: 53–60.
4. Stanley JR, Amagai M. Pemphigus, bullous impetigo, and the staphylococcal scalded-skin syndrome. *N Engl J Med* 2006; 355: 1800–1810.
5. Rieger-Fackeldey E, Plano LR, Kramer A, Schulze A. Staphylococcal scalded skin syndrome related to an exfoliative toxin A- and B-producing strain in preterm infants. *Eur J Pediatr* 2002; 161: 649–652.
6. Hoffmann R, Lohner M, Bohm N, Schaefer HE, Leititis J. Staphylococcal scalded skin syndrome (SSSS) and consecutive septicaemia in a preterm infant. *Pathol Res Pract* 1994; 190: 77–81.
7. Makhoul IR, Kassis I, Hashman N, Sujov P. Staphylococcal scalded-skin syndrome in a very low birth weight premature infant. *Pediatrics* 2001; 108: E16.
8. Tenenbaum T, Hoehn T, Hadzik B, Stannigel H, MacKenzie CR, Mayatepek E, Schroten H. Exchange transfusion in a preterm infant with hyperbilirubinemia, staphylococcal scalded skin syndrome (SSSS) and sepsis. *Eur J Pediatr* 2007; 166: 733–735.
9. Plano LR, Adkins B, Woischnik M, Ewing R, Collins CM. Toxin levels in serum correlate with the development of staphylococcal scalded skin syndrome in a murine model. *Infect Immun* 2001; 69: 5193–5197.
10. Blyth M, Estela C, Young AE. Severe staphylococcal scalded skin syndrome in children. *Burns* 2008; 34: 98–103.
11. Becker DS. Toxic epidermal necrolysis. *Lancet* 1998; 351: 1417–1420.