Staphylococcal Scalded-Skin Syndrome Complicating Wound Infection in a Preterm Infant with Postoperative Chylothorax

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The course of infection in a 3-week-old premature newborn suffering from extensive dermatitis with flaccid blisters is described. Staphylococcus aureus was recovered from a local wound infection around a chest tube inserted to drain a postoperative chylothorax. The strain isolated tested positive for the eta gene for exfoliative toxin A, the causative agent of staphylococcal scalded-skin syndrome (SSSS). In this case, prematurity and loss of chylus with consecutive lymphopenia may have contributed to development of SSSS.

Systemic findings and generalized involvement leading to the clinical appearance of scalded skin were the hallmarks of the staphylococcal scalded-skin syndrome (SSSS). It is caused by one of the two exfoliative toxins (ETs) exfoliatin A (ET-A) and ET-B, which are produced by certain strains of Staphylococcus aureus and which lead to intraepidermal cleavage. Newborns and infants younger than 5 years of age are predominantly affected (13). SSSS is typically associated with a trivial infective focus in the nasopharynx, conjunctivae, the skin, the inner ear, the umbilicus, or the urinary tract (13). Reports of SSSS following postoperative wound infection are rare (1, 2). We report an unusual case of a premature infant operated on for an esophageal interruption complicated by postoperative chylothorax (accumulation of lymphatic liquid in the pleural space) and subsequent development of SSSS. ET-A-producing S. aureus was cultured from a local wound infection around a chest tube.

Case report. The boy (gestational age, 34 weeks; birth weight, 1,695 g [3 lb 12 oz]) was admitted to the neonatal intensive care and diagnosed with esophageal interruption. Four hours after birth, the malformation was corrected by surgery. The postoperative course was complicated by chylothorax of the right side, leading to respiratory insufficiency 14 days after the operation. A no. 8 French chest tube (XRO trocar drain no. 625; Vygon, Ecouen, France) was placed for drainage of fluid. Twenty-five milliliters of a milky yellowish fluid containing 2.1 g of protein per dl, 648 mg of triglycerides per dl, 57 mg of cholesterol per dl, and 22,500 nucleated cells/mm³ containing 95% lymphocytes (all values indicative for chylus) was aspirated. Culture of drainage fluid yielded no growth, but from subsequent development of SSSS. ET-A-producing S. aureus was cultured from a local wound infection around a chest tube.

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The C-reactive protein was normal. The clinical picture was interpreted as SSSS, and prophylactic intravenous treatment with fluocoxacillin (100 mg/kg of body weight/day in three doses) was started 8 h after onset of blistering. The supportive care of the patient consisted of fluid replacement, substitution of protein loss, antiseptic dressing, analgesic treatment, and aseptic care. An incubator was used to help maintain the infant’s body temperature. Despite rapid improvement in general condition, the boy’s skin continued to exfoliate for the first 3 days after antibiotic treatment had been started. Most areas of the skin were reepithelialized after 8 days, and complete resolution without scarring was noted within 14 days. The chylothorax did not relapse, and the infant was discharged to home after 59 days.

Bacteriology. Blood cultures yielded no growth, but from cultures of the purulent drainage around the catheter, S. aureus was isolated on Columbia blood agar. The isolate was a coagulase-positive strain with typical colony morphology. The antimicrobial susceptibility testing was done by microdilution according to the “Deutsche Industrie-Norm” (German industrial norm). The strain was a typical methicillin-sensitive S. aureus strain, for which there were the following MICs: penicillin G, >1 mg/liter (resistant); oxacillin, 0.25 mg/liter; gentamicin, 0.25 mg/liter; ceftoxacin, 0.125 mg/liter; erythromycin, 0.25 mg/liter; clindamycin, 0.125 mg/liter; vancomycin, 0.5 mg/liter; teicoplanin, 0.25 mg/liter; and rifampin, 0.125 mg/liter (all sensitive).

For phage typing, the international basic set of phages typing S. aureus was used; the methodology corresponds to that of Blair and Williams (3). The strain could not be phage typed.

For PCR of exfoliative toxin genes eta and etb, primers and PCR mixes were used as previously described by Johnson et al. (15); the annealing temperature was 55°C. The strain was shown to possess the eta gene for ET-A production but no etb (ET-B) determinant (Fig. 2A).

Genotyping of S. aureus by using Smal macrorestriction analysis (pulsed-field gel electrophoresis) was performed as
of ET-A and ET-B have been determined by several groups (15, 16). Approximately 5 to 6% of *S. aureus* strains are ET producers, with over 80% of the ET as ET-A (22). *S. aureus* strains with a capacity for ET formation have been described as a separate clonal group, as already suggested by their common phage pattern, including phage 71 (20).

The diagnosis of SSSS can be confirmed by recovery of group II staphylococci. Blisters and erosions frequently yield no organisms when sampled for bacterial cultures, and blood cultures are usually sterile. Strains isolated from local bacterial foci may be phage typed to determine epidemiological relatedness, since most toxigenic strains of *S. aureus* are identified by group II phage (types 71 and 55), but other phage types have been implicated (7, 8). However, the limits of phage typing become obvious when the corresponding strain is revealed as nontypeable. Although *S. aureus* strains exhibiting group II phage patterns (including phage 71) exhibit related *SmaI* restriction patterns, they may not necessarily possess the *eta* gene (25). The strain in the present case of SSSS was nontypeable by phages, and its *SmaI* macrorestriction pattern was different from that of reference strain 1634/97; however, the *tar916-shida-PCR*, a quite different method of molecular population analysis (6), suggests a relatedness and a probable descent from this clonal group.

SSSS is predominantly a disease of infancy and early childhood, with only a few adult cases reported (5). In the neonate, the usual onset is between days 3 and 16 of age (7), and a congenital case has been reported (17). Only six cases of SSSS in premature infants have been described (10, 14, 25), although newborn nurseries and neonatal intensive care units are at risk for outbreaks of SSSS (7, 8, 25). Nursing staff infected or colonized with ET-producing *S. aureus* are typically the source of such outbreaks (25). Factors responsible for the age distribution include renal immaturity leading to decreased toxin clearance in neonates (11) and lack of immunity to the toxin (13). The percentage of carriers of antibody to ET-A decreases from 88% immediately after birth to a minimum of 30% at 4 months to 2 years and then rises again (13). The age of our patient was 4 weeks at onset of SSSS. Thus, lack of transplacental ET-A antibodies due to nonimmunity of the mother as well as decreasing antibody titers may have contributed to SSSS in our patient. Antibody levels are relatively low in premature infants compared to those in full-term babies, and this could have been an additional pathogenic factor for development of SSSS in our case.

SSSS as a complication of wound infection has been rarely described for neonates (1, 2) and has never been found in combination with chronic loss of lymphocytes. Drainage of chylothorax may cause immunodeficiencies, including abnormal cell-mediated immune response (19). Patients with chylothorax are lymphopenic and demonstrate depressed relative and absolute numbers of helper and inducer T cells (CD4), normal to increased relative numbers of cytotoxic and suppressor T cells (CD8), and a reversed CD4/CD8 ratio (4, 12). Some patients show a reduced proliferative response of peripheral blood mononuclear cells to mitogens (4, 12). These findings may partially explain abnormal cellular and humoral immunity in patients with chylothorax and may account for the development of SSSS in our patient, since the lymphocyte count of the presented infant was at an absolute minimum at onset of SSSS. Similar findings have been reported in an adult patient with acquired immunodeficiency syndrome who developed SSSS and had a pattern of T-cell levels seen with loss of chylus (23).

Conclusions. In addition to the typical clinical picture, detection of ET is required for diagnosis of SSSS. The identification of ET-A and ET-B genes in strains of *S. aureus* by PCR.
offers a reliable, rapid, and inexpensive method for detection of toxigenic strains (15). An immature immune system predisposes the preterm neonate to infection (20, 26, 28). Transient weakening of the immune system by loss of lymphatic fluid accompanies chylothorax. The combination of both conditions may increase susceptibility to SSSS if infants have been colonized with ET-producing S. aureus. Studies of lymphocyte subpopulations and functional lymphocyte testing may help to further elucidate the pathogenesis of SSSS in the future.

REFERENCES