

## STAPHYLOCOCCAL SCALDED SKIN SYNDROME IN AN ADULT WITH FATAL DISSEMINATED STAPHYLOCOCCAL SEPSIS

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**Abstract.** The case of a 63-year-old man with a staphylococcal scalded skin syndrome as the first clinical manifestation of a disseminated staphylococcal sepsis is reported. The findings of the histological, electron microscopical and bacteriological investigations are presented and the possible reasons for the fatal outcome are discussed.

**Key words:** Staphylococcal scalded skin syndrome in an adult; Staphylococcal sepsis

The staphylococcal scalded skin syndrome (SSSS) usually occurs in children under 6 years of age whose skin and/or mucosa have been colonized by *Staphylococcus aureus* which produces a toxin that induces a superficial cleavage in the granular layer of the epidermis. The most important differential diagnosis is drug-induced toxic epidermal necrolysis (TEN) which is usually considered to be a disease of adults, but does occasionally occur in children (1, 4, 5, 8, 9, 12). Rarely, SSSS may also occur in adults who have been treated with immunosuppressive agents or have impaired renal function and invariably exhibit septic abscesses, septicemia or pneumonia. Naturally, the mortality of these patients is high (9, 11). The aim of this study is to report a new case of SSSS in an adult who, in addition to the usually skin lesions of SSSS, developed metastatic septic skin lesions due to *Staphylococcus aureus*.

### CASE REPORT

A 63-year-old male was admitted to our department suffering from a sudden onset of erythema with generalized exfoliation, superficial erosions and flaccid blisters on the face and trunk. Prior to admission the patient had been treated for severe esophageal stenosis and had received parenteral nutrition via a right internal jugular line for 3 weeks before onset of the skin lesions. The patient was in a cachectic state; he was afebrile before and during admis-

sion. The skin of the face, dorsal parts of the trunk and regions of the upper extremities exhibited superficial exfoliation with scattered erosions (Figs. 1, 2 A). The adjacent uninvolved portions of the skin exhibited a slight erythema and were icteric as were the sclerae. Nikolsky's sign was positive in the involved and apparently uninvolved areas and the diagnosis of SSSS was established by exfoliative cytology (4, 5) which showed acantholytic cells. Pemphigus foliaceus was ruled out by direct and indirect immunofluorescence. Sequential blood cultures were positive for Gram-positive cocci, which were later identified as *Staphylococcus aureus* (see Results). Multiphasic screening panel revealed an elevated BUN (47 mg/100 ml) and creatinine (1.8 mg/100 ml). Bilirubin was elevated to 4.56 mg/100 ml, hematocrit was 35%, WBC was 6 500 and there was thrombocytopenia of 43 000.

Treatment consisted of oxacillin 4 g t.i.d. and piperacillin 4 g t.i.d. On account of the patient's critical state, continuous monitoring of the central venous pressure (CVP), cardiac and urinary output and serial blood determinations of glucose, BUN and electrolytes was performed. Fluids, electrolytes, proteins and caloric supply, as well as fresh blood and fresh frozen plasma were given as needed. Several hours after antibiotic treatment was initiated, the body temperature rose to 40°C. New skin lesions in the form of flaccid blisters appeared and the condition of the patient rapidly deteriorated into a progressive septic shock which necessitated additional treatment with methyl-prednisolone 1 g b.i.d. and 5 g gamma-globulin i.v.

The patient developed an exanthematic rash consisting of small purpuric papules and vesicles with a predominance in the lower extremities (Fig. 2 B). Biopsies of these lesions revealed vasculitis, massive inflammation and cocci which were also seen by electron microscopy (see Results) (Fig. 4). At the end of the second day, blood pressure and body temperature fell rapidly, CVP rose, and anuria as well as respiratory insufficiency developed. A chest X-ray disclosed disseminated pneumonic infiltrations in both lungs. BUN reached 85 mg/100 ml, creatinine was 2 mg/100 ml. Bilirubin 5.7 mg/100 ml. SGOT, SGPT and  $\gamma$ -GT were also elevated. Blood glucose was 360 mg/100 ml. The patient expired one hour after anuria was diagnosed, despite intensive additional treatment with dopamine, furosemide in high dosage, and ethacrinic acid, as well as oxygen administration.



Fig. 1. Exfoliation and erosions on the face.

## RESULTS

### *Exfoliative cytology*

Smears were taken from recently developed erosions and stained by Giemsa. Both nucleated and anucleated acantholytic keratinocytes were seen, in addition to small groups of epidermal cells that were in contact with one another. No inflammatory cells, cellular debris, or cuboidal epithelial cells were seen in the specimens.

### *Histopathology*

A cleft formation within the stratum granulosum was seen on paraffin sections stained with H and E. The underlying malpighian layer of the epidermis was completely intact. The roof of the blister was formed by the stratum corneum and some granular cells (Fig. 3). A few acantholytic granular cells were present within the cleft. The dermis contained no inflammatory cells and, apart from a widening of the blood vessels, was normal. Direct and indirect immunofluorescence was negative for both in vivo bound and circulating immunoglobulins.

### *Electron microscopy*

Ultrastructural examination of a biopsy taken from an area immediately adjacent to an erosive lesion

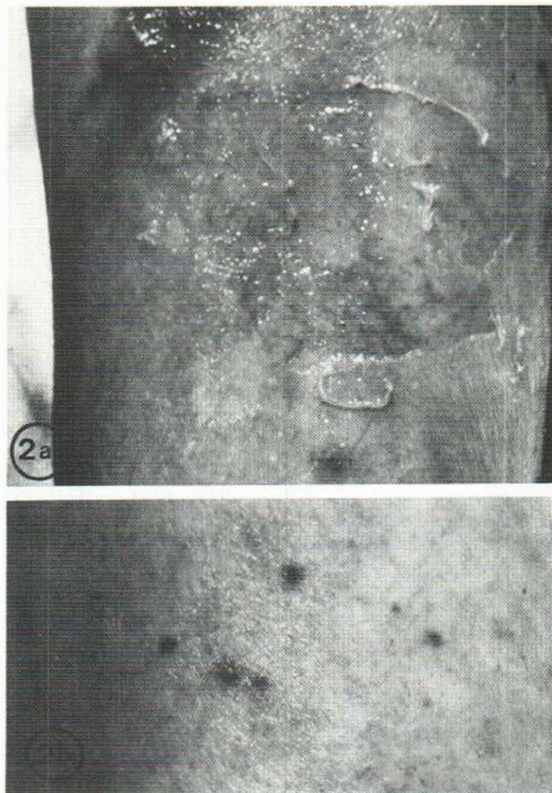


Fig. 2. (A) Large erosive areas on the arm. (B) Purpura-like septic skin lesions on the thigh.

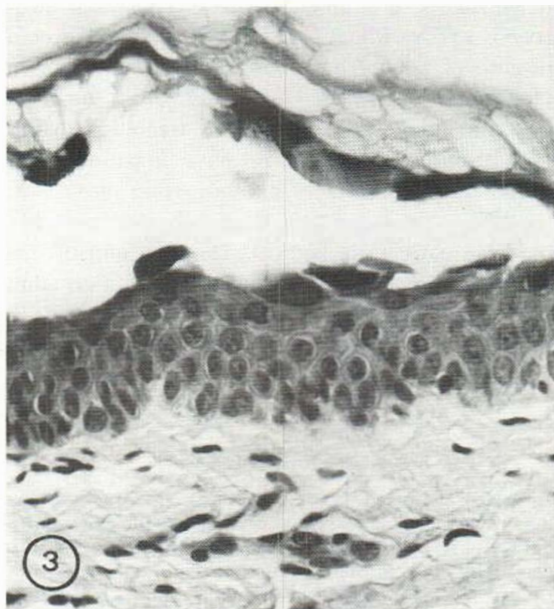


Fig. 3. The cleavage plane between the horny layer and the malpighian layer runs through the granular layer.

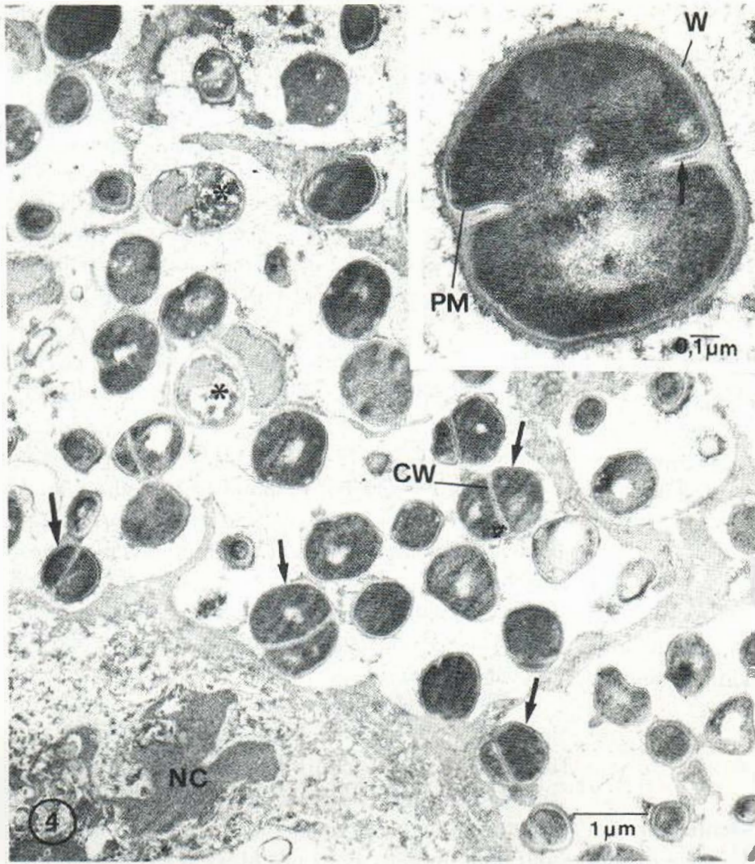


Fig. 4. Electronmicroscopy of purpura-like septic skin lesion (see Fig. 2b). Microabscess with masses of staphylococci trapped in a network of cellular debris. Both single and dividing staphylococci (arrows) are present. CW cross wall. Some of the bacterial organisms exhibit signs of degeneration (\*). NC, necrotic cell at the border of the microabscess  $\times 12\,150$ . Inset: Staphylococcus with characteristic cell wall (W) and plasma membrane (PM) (12). Arrow: Formation of cross wall.  $\times 42\,000$ .

revealed a cleavage at the interface of the stratum granulosum and the upper stratum spinosum. The cell membranes of the cells bordering the cleavage space were intact. Cleaved half-desmosomes were seen bordering the cleavage space. Another biopsy from a purpuric papular lesion of the thigh revealed vasculitis, small vessel thrombosis and focal ac-

cumulation of bacteria within the papillary dermis. The bacterial organisms were surrounded by necrotic cells and unidentifiable debris. These organisms were also present, phagocytosed in adjacent macrophages. The ultrastructural features of these bacteria corresponded to those of staphylococci (14) (Fig. 4).

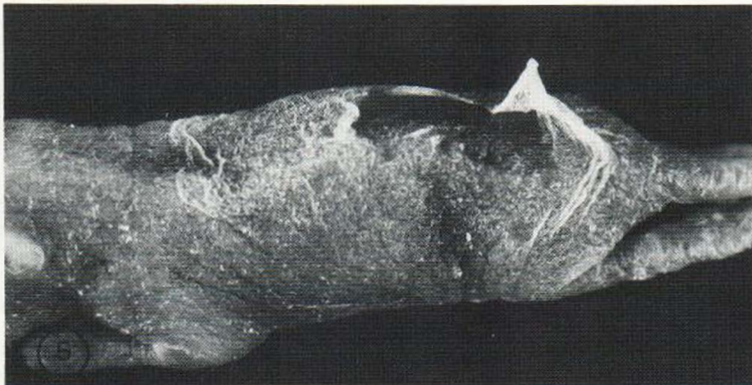


Fig. 5. Experimental reproduction of the skin lesions by injection of the toxin into a newborn mouse.

### Bacteriological investigations

Multiple blood cultures revealed growth of *Staphylococcus aureus*. The same bacteria were recovered from eroded skin blisters. This *s. aureus* strain was further characterized. It appeared to be a  $\beta$ -lactamase producer, and was positive for Protein A (2). Phage typing showed the staph. strains to belong to phage group II (3A $\pm$ /3c $\pm$ /55 $\pm$ ) (phage typing kindly done by W. LenZ, M.D., Bonn-Venusberg, (Germany). The epidermolytic toxin production of this strain was proved in the newborn mouse model in that newborn mice injected subcutaneously with 10<sup>8</sup> cocci developed generalized exfoliation (1, 9) (Fig. 5). Antibodies against staphylococcal teichoic acid were not demonstrated in the patient's serum when employing the method of Nagel et al. (10).

### Necropsy findings

Benign esophageal stenosis, parietal thrombosis of superior vena cava, septicopyemia, metastatic pyemic abscesses in lungs, heart, kidney, spleen and skin; SSSS.

## DISCUSSION

Rapid and definitive diagnosis is essential in the management of patients with SSSS because of the different mode of treatment of SSSS and drug-induced TEN. SSSS necessitates high dosage antibiotic treatment—but not steroids, as would be the case in TEN (8, 9, 10, 11, 12).

The fact that SSSS occurs almost exclusively in young children may be explained by a decreased capacity of children to metabolize or excrete the toxin, or by a more mature immunological response to staphylococcal infection in adults. There are several clinical manifestations of SSSS (1, 9): localized or generalized bullous impetigo, or generalized scarlatiniform erythroderma and generalized exfoliation. This variable clinical picture apparently depends upon the severity of the staphylococcal disease and the varying capacities of different stains of staphylococci phage II (III), to produce exfoliatin (1, 2, 3, 7, 9).

In contrast to the relatively benign nature of the initiating staphylococcal infection in most children, adult patients have severe staphylococcal disease and widespread exfoliation. The onset of this generalized form is usually dramatic, characteristically appearing first as diffuse erythema on the face,

neck and groin, followed within 24–48 hours by extensive erosions on pressure points and the appearance of generalized flaccid bullae over much of the body. In children, severe systemic toxicity is usually absent and there is relative sparing of the mucosal surfaces; complete healing without scarring usually occurs within days and the mortality rate is low. In contrast to this, the prognosis of the adult SSSS is poor because of a compromised host due to severe systemic illness. The reasons why our patient developed SSSS are quite apparent: A contaminated catheter seems to have been the port of entry for staphylococcal infection in a malnourished patient, as has been previously observed by Sanders & Sheldon (1976) (13).

The patient did not respond to this infection in the usual manner with fever and leukocytosis. Later widespread staphylococcal organ involvement produced high levels of epidermolytic toxin which led to the development of SSSS so that the skin manifestations were the first clinical sign of staphylococcal septicemia.

It appears that appropriate therapy was begun too late; i.e., at a stage when the infection had already involved multiple organs (heart, lungs, kidneys) and this corresponds to the observations that in experimental animals with advanced systemic infection antibiotic therapy does not prevent exfoliation and death (9). Clearly, the administration of corticosteroids in our patient aggravated exfoliation and we would therefore advocate steroid therapy in SSSS only in those rare instances where septic shock and/or a respiratory distress syndrome have developed. Another factor which contributed to the fatal outcome in our patient may have been terminal renal insufficiency (6, 11) which probably prevented adequate renal excretion of the epidermolytic toxin.

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