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Relapsing bullous staphyloderma

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Relapsing eruptions of bullae rapidly turning into pustules were seen in a 69-year-old woman of good general health. At different times during several months of observation, strains of *S. aureus* were grown from various lesions, including one (phage group III) producing enterotoxin C. Systemic involvement except for high BSR was absent and repeated blood cultures were negative. Histopathological findings resembled impetigo. Antibiotic treatment was effective. As this disease does not fit into any of the well-known pustular infectious dermatoses, we suggest calling it relapsing bullous staphyloderma. ***Key words: Staphylococcus aureus; Enterotoxin C; Impetigo.***

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CASE REPORT

History

A 69-year-old woman in good general health came to us with a 1-year history of pustular skin eruptions which had rapidly worsened during the last week prior to admission. The patient had not been seriously ill in her life and had given birth to two healthy children.

Clinical features

On admission, the skin was covered with disseminated pustules and erosions surrounded by marked erythema (Fig. 1). All body areas except the face, palms, soles and mucous membranes were affected. New lesions developed continuously during the following days. Initially these consisted of small vesicles with an erythematous rim, which rapidly turned into large flaccid pustules spreading centrifugally. The pustules had a tendency to coalesce and were easily disrupted, leaving weeping or crusted circinate erosions (Fig. 2). The Nikolski sign was negative. Healing of individual lesions, without scarring, was complete after approximately 10 days.

One week after cessation of therapy, fresh pustules reappeared on the trunk. As before, there were no signs of systemic illness.

Microbiology

For microbiological investigations, intact pustules were thoroughly cleansed, disinfected and subsequently punctured. Strains of γ-hemolytic *S. aureus* (phage group III; 47; 54; 75; 85 ± 77) were isolated from different pustules located on the trunk and the extremities.

During the first relapse, identical strains of γ-hemolytic *S. aureus* (phage group I/III/M;79/53/54/77/84/85/95) were recovered from pustules in different locations on the trunk, from the scalp and the nasal mucosa. Blood cultures were repeatedly sterile. Gram-stained smears of aspirated pustule content (pus) showed, besides numerous neutrophils, keratinocytes with adherent Gram-positive cocci.

Isolated strains of *S. aureus* (phage group I/III/M) were subsequently examined for production of toxins. The only toxin found was enterotoxin C. Epidermolytic toxin A, epidermolytic toxin B, toxic shock toxin or further enterotoxins were absent.

Light microscopical findings

A skin biopsy from the chest was obtained, showing a subcorneal pustule and a slightly spongiotic epidermis. The pustule contained numerous neutrophils as well as a few acantholytic keratinocytes. In addition numerous neutrophils were located throughout the upper dermis and in the perivascular region a lymphohistiocytic infiltrate was present (Figs. 3, 4). Direct immunofluorescence staining proved negative.

Ultrastructural observations

Ultrastructural observations of the lower epidermis showed spongiosis as well as numerous apparently intact neutrophils between the keratinocytes. The base of the pustule was formed by flattened keratinocytes of the granular layer and was overlaid by neutrophils. These neutrophils showed varying degrees of necrosis together with partial to complete extrusion of intracellular material, especially azurophilic and specific granules. Within the blister fluid, acantholytic and partially

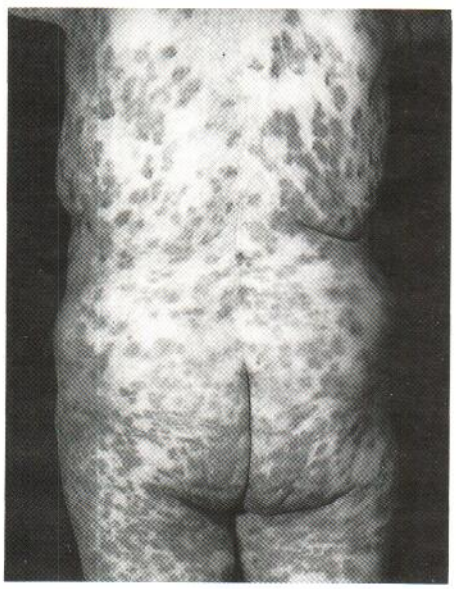

Fig. 1. Multiple disseminated pustules and erosions covering the trunk and extremities.

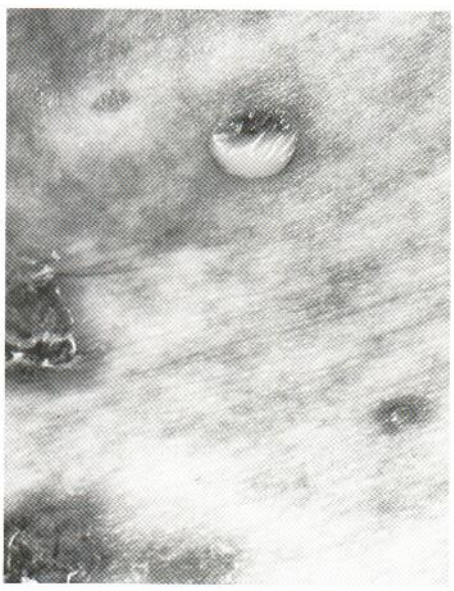

Fig. 2. Flaccid pustules on erythematous skin with pus accumulating in their lower half. Crusted erosions due to destruction of pustules.

Fig. 3. (left) Histopathology of a fresh lesions: Part of a subcorneal pustule in a slightly acantholytic spongiotic epidermis. Perivascular lymphohistiocytic infiltrate, also with some neutrophils in upper and middle dermis.

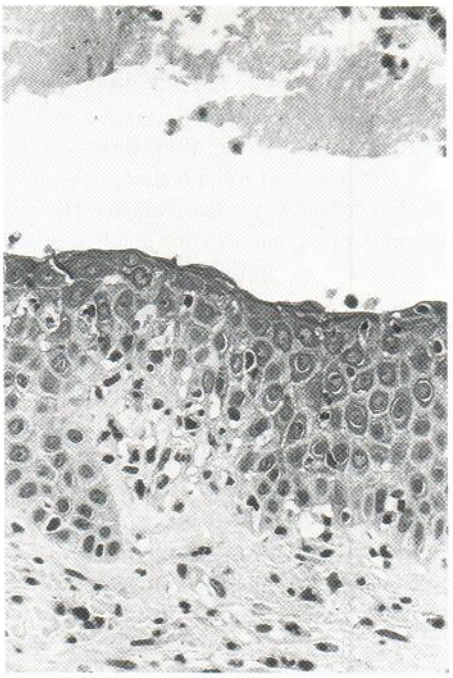

Fig. 4. (right) Base of subcorneal pustule, with polymorphonuclear neutrophils migrating through the epidermis.

necrotic keratinocytes were surrounded by neutrophils in different stages of phagocytosis. In some of these neutrophils, degranulation into large phagocytic vacuoles was observed, so that the cytoplasm was nearly devoid of typical granules.

Laboratory parameters

Routine laboratory parameters were inconspicuous except for a constantly elevated BSR (70/101 mm), positive C-reactive protein, and positive rheumatoid factor. During the first course of therapy, these pathologic changes normalized, though after the reappearance of pustules, BSR again became elevated, to approximately 50/90 mm.

IgE was 229 U/ml, the T4 : T8 ratio was 1.0, the score in the Merieux Multitest was 9. There were normal values for routine laboratory parameters and for plasma levels including glucagon, insulin, cortisol, glucose-6-phosphate-dehydrogenase, T3, T4, antistaphylolysine, antistreptolysine, carcinoembryonic antigen, α-fetoprotein, C2, C4, immunoelectrophoresis, antinuclear antibodies. HLA B8 was positive; HLA-Cw6, B13, B17, B27 were negative.

Leukocyte function tests

Functional activities of neutrophils obtained at the same time from pustules and peripheral blood were repeatedly investigated. The results of this study are described elsewhere (1).

Treatment

The first course of treatment, with 2 g oxycillin i.v. daily for 10 days, resulted in complete clearing of the lesions. When fresh pustules occurred, the same therapy was given but this time with only limited success. The patient was therefore given ofloxacin 400 mg per os, which gave a marked clinical improvement. After nearly complete clearing, the patient was dismissed and no further treatment was given.

Follow-up

Six months later the patient returned to the hospital for re-examination. There were a few fresh pustules on trunk and extremities. Several cultures grown from pustule contents were sterile, although cocci could be identified in Gram stains. *S. aureus* was successfully recovered from scalp and nasal swab (β-hemolytic, phage groups I/III/M; 79/53/54/77/84/85/95). BSR was 40/70 mm and routine laboratory parameters were normal. No treatment was initiated.

Finally, pustules formation no longer took place and the patient was in good health, the BSR was normal (3/10 mm). Her condition has remained stable now for 3 years.

DISCUSSION

In this report an elderly patient is described suffering from widespread pustular eruptions on the trunk, most likely due to *S. aureus*. Histology revealed subcorneal accumulation of granulocytes and numerous neutrophils were located between epidermal cells as well as within the pustules. There were no signs of systemic illness except for a highly elevated BSR and positive early-phase reactants (e.g. C reactive protein, rheumatoid factor) all of which of which turned to normal after clinical clearing.

At first sight the clinical picture could resemble pustular psoriasis, pemphigus, migratory necrolysis with glucagonoma, subcorneal pustulosis, or impetigo contagiosa. However the present case could be clearly distinguished from these dermatoses by the clinical picture, histology with absence of spongiform pustules (for pustular psoriasis), lack of immunoglobulin deposition by direct immunofluorescence (for pemphigus), and normal plasma level of glucagon, insulin and glucose (for glucagonoma syndrome). In addition, at two different times during the illness, virtually identical strains of *Staph. aureus* (γ-hemolysin, phage group I/III/M) were recovered from the pustules.

Identification of *S. aureus* in pustule contents as well as the patient's prompt response to antibiotic therapy make it likely that bacterial colonization was the cause of this disease. The condition would thus resemble impetigo, except that the lesions occurred at the unusual age of 69 and consisted in disseminated lesions on the trunk, sparing face and skin folds.

Whereas classical impetigo contagiosa is clearly different, staphylococcal scalded skin syndrome (SSSS) shows resemblence in depicting a similar histopathological picture (2), occurrence in adults (3, 4, 5), and showing *S. aureus* as the

causative agent. However, though bullae may occur in SSSS (6), the presence of disseminated flaccid pustules is not typical for SSSS and, more importantly, production of the epidermolytic toxins characteristic for SSSS was absent in our patient.

Relapses occurring after various intervals could resemble reinfections from still infected body sites or known habitats of *S. aureus* such as the nasal mucosa. In fact the latter represents a well known reservoir for staphylococcal infections (7). This assumption is supported by the fact that the same toxin-producing strain (phage group I/III/M) identified in pustules was recovered from the nasal cavity in our patient.

S. aureus is considered one of the most common bacterial pathogens encountered in hospitals as well as at large, and skin diseases caused by *S. aureus* are well known (7, 8). Conditions which are related to the production of staphylococcal toxins include SSSS (6) as well as toxic shock syndrome (TSS) (9, 10), in which epidermolytic toxins A and B and toxic shock toxin 1 resp. were found responsible. Little is known, however, concerning the role of staphylococcal enterotoxins in skin disease (11, 12, 13, 14). Enterotoxin C was found to be produced by appr. 18% of *S. aureus* strains isolated from clinical specimens (15) and, in combination with other toxins, was associated with exfoliative dermatitis (13) and toxic shock syndrome (12, 14). Nevertheless the pathogenic relevance of enterotoxin C in skin disease still remains to be determined.

Taken together, there are several unusual features seen in this patient suffering from a bacterial skin disease due to *S. aureus*. The infection was confined to the subcorneal zone of the skin with an eruption of flaccid bullae that rapidly turned into pustules. Despite whole body involvement, systemic signs of illness were absent except for elevated BSR and acute-phase proteins. Enterotoxin C was the only enterotoxin produced by a *S. aureus* strain (phage type I/III/M) and the clinical picture does not appear to fit into any of the known infectious pustular dermatoses.

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