Clinical Case of the Month

Staphylococcal Scalded Skin Syndrome: A Rare Complication of a Common Pathogen

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A 45-year-old African-American woman presented to the emergency department with complaints of fever without chills and musculoskeletal back pain radiating down both legs that had begun two days prior to presentation. Initial radiographs revealed lumbar spondylolisthesis. The patient was evaluated, given an unknown muscle relaxant, and discharged from the emergency department. The patient returned two days later with similar complaints including progressive lower back pain radiating down her legs which restricted ambulation.

The patient's past medical history included non-insulin dependent diabetes mellitus and hypertension. Her surgical history was significant for a partial hysterectomy several years prior to presentation. She denied smoking, alcohol consumption, or illicit drug use of any type.

After returning to the emergency department, the patient underwent extensive evaluation, including lumbar puncture. The patient was admitted and empirically treated with vancomycin, rifampin, and cefotaxime. Blood cultures and CSF cultures demonstrated the presence of methicillin resistant *Staphylococcus aureus* (MRSA). She received a 21-day-course of vancomycin and rifampin for MRSA meningitis. The patient improved clinically and follow-up was arranged with a home-health nurse and a home physical therapist. Three days prior to discharge, a pemphigoid-type rash developed on her right arm, for which a petrolatum-based ointment was prescribed.

One week after discharge, the patient presented to the emergency department with a severe desquamating rash, diffuse body aches, and dehydration. She described the rash as starting on her right upper extremity and spreading globally, only sparing mucous membranes, soles of feet, and palms of hands.

Physical examination revealed an afebrile patient with stable vital signs and a diffuse desquamating rash, with underlying normal skin, extending from the occiput to knees bilaterally (Figures 1 and 2). Nikolsky's sign was present over seemingly unaffected skin. No oral, conjunctival, or vaginal lesions were noted. Cardiovascular, pulmonary, and abdominal exams were within normal limits.

Upon admission, laboratory studies revealed a leukocyte count of 28,000 (normal range, 4.5-11.0 x 10^3 wbc per μL) along with a hemoglobin of 9 (normal range, 12.0-16.0 g/dL) with normal indices and a slightly elevated platelet count. Erythrocyte sedimentation rate was

CME Information

Target Audience

The November/December Clinical Case of the Month is intended for primary care physicians, general internists, dermatologists, and infectious disease physicians.

Educational Objectives

After reading the article, the healthcare provider should be able to discuss the differential diagnosis and management of Staphylococcal Scalded Skin Syndrome.

Estimated time to complete this activity is 1 hour.

Credit

The LSMS Educational and Research Foundation designates this educational activity for a maximum of one (1) *AMA PRA Category 1™ Credit*. Physicians should only claim credit commensurate with the extent of their participation in the activity.

Disclosure

Dr. Ahuja has nothing to disclose.
Dr. Hrom has nothing to disclose.
Dr. Woods has nothing to disclose.
Dr. Brown has nothing to disclose.
Dr. Lopez discloses that he is a member of the *Journal* Board of Trustees and the *Journal* Editorial Board.

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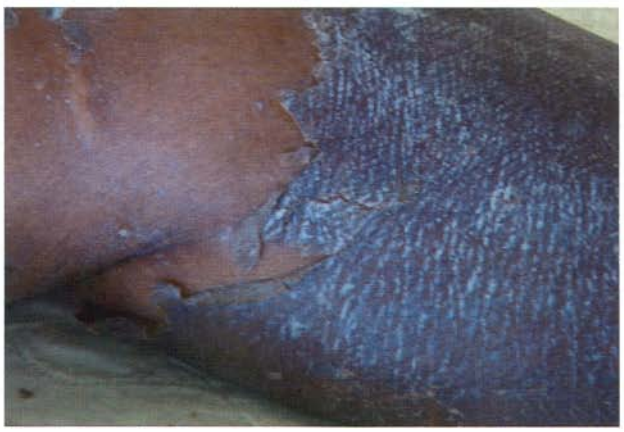

Figure 1. Sloughing of the epidermis of the leg.

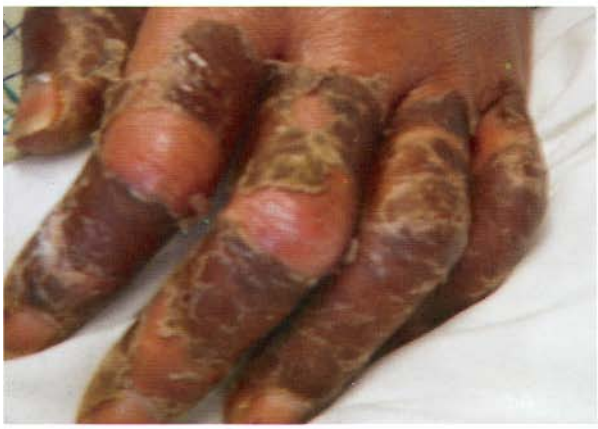

Figure 2. Degloving of skin of the hand on hospital day 2.

95 (normal range, 1-9mm/hr), and C-reactive protein level was 30 (normal range, 0-0.9 mg/dL. Chemistries were normal except for a BUN/Cr ratio of 136/2.3 (normal range, BUN: 7-18 mg/dL, Cr 0.6-1.2 mg/dL). Hansel's stain of urine showed rare to occasional eosinophils. Serology demonstrated the presence of antibody to hepatitis C.

The patient was admitted to the general medicine service. A skin biopsy showed subcorneal splitting along the granular layer without dermal infiltration consistent with Staphylococcal Scalded Skin Syndrome (SSSS) (Figure 3). No organisms were present within the biopsy specimen. MRSA was isolated from multiple blood cultures. Transesophageal echocardiogram revealed no evidence of infective endocarditis.

A repeat lumbar puncture was not performed secondary to the patient's overlying skin desquamation. She was treated with a 21-day-course of vancomycin, cefepime, and rifampin. In addition, she received wound care and intravenous hydration. Antibodies to TSST-1 and staphylococcal enterotoxin B were present. Laboratory studies searching for the presence of exfoliative toxins A and B were negative. The patient's skin rash slowly resolved without scarring.

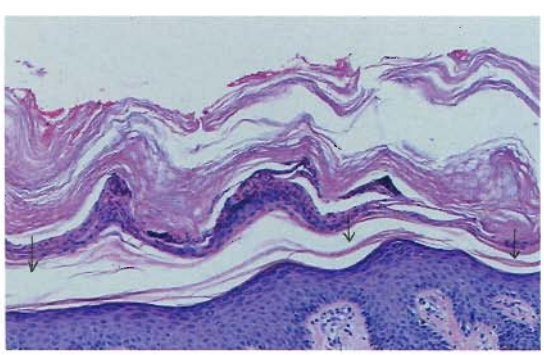

Figure 3. Histologic section of skin biopsy stained with hemotoxylin and eosin reveals subcorneal splitting along the granular layer without dermal infiltration (arrows). No organisms are present.

DISCUSSION

With only approximately fifty cases reported, SSSS is rarely seen in adults. To our knowledge, only three cases of MRSA-associated SSSS have been documented, and none involved MRSA meningitis. SSSS typically affects neonates and young children, likely secondary to the presence of immature renal clearance capabilities and naïve immune systems. Adults that are vulnerable to SSSS are typically immunocompromised, eg, by HIV, cirrhosis, or diabetes mellitus. Immunosuppression results in overproduction of toxin by the bacteria. In addition, most adult cases involve patients with some degree of renal insufficiency, resulting in reduced elimination of the toxin.[1] The ages of affected adults reported range from 19-91 years, with 50% of them over 60.

SSSS is a toxin-mediated type of exfoliative dermatitis caused by strains of *Staphylococcus aureus* which produce exotoxins A and B. Nearly ninety percent of cases reported in children involve exotoxin A.[2] Conversely, exotoxin B is isolated more frequently in adult cases of generalized SSSS. Exotoxin B is thought to be more virulent.[2] These exfoliative toxins cleave the cell adhesion molecule desmoglein 1, resulting in interruption in the epidermis and widespread desquamation. In a case similar to ours, there was no demonstratable serologic evidence of exotoxins A and B, but the toxic shock syndrome toxin-1 (TSST-1) and enterotoxin produced by methicillin-resistant *S. aureus* were both present.[3] Multiple cases of SSSS report the presence of an enterotoxin or TTST-1 in the absence of demonstratable evidence of exotoxins.[3]

In patients affected by SSSS, a prodromal infection typically originates in the nose, mouth, throat, skin, umbilicus, or surgical wound. *Staphylococcus aureus* may be cultured from the suspected site of infection although the resulting bullae are generally culture-negative.[4] In some cases, the infection remains superficial and localized; in others the toxin enters the bloodstream and may produce sepsis. SSSS patients usually experience signs and symptoms in a predictable order of events: fever,

erythema of the skin, and edema in the epidermis, resulting in bullous lesions that separate easily in the presence of gentle rubbing. This latter phenomenon is referred to as a positive Nikolsky's sign. Importantly, in SSSS the mucous membranes are always spared. The affected areas gradually crust over, resulting in widespread desquamation which is quite painful.

The diagnosis of SSSS is made by considering clinical, microbiological, and histological criteria including: positive cultures revealing *S. aureus* from sites other than blisters or exfoliated locations, the presence of toxins produced by the bacteria, skin biopsy with characteristic intraepidermal cleavage, and a clinical pattern consistent with the syndrome.[5] Skin biopsy reveals subcorneal splitting along the stratum granulosum without dermal infiltration, bacterial organisms, or inflammatory cells.

When considering the differential diagnosis, the list of possibilities includes drug hypersensitivity reactions, particularly toxic epidermal necrolysis (TEN), viral-associated exanthems, and scarlet fever. One important distinction between SSSS and TEN is that TEN involves mucous membranes while SSSS does not. Another helpful diagnostic clue is the presence of pain associated with the rash of SSSS. Bullous impetigo is caused by the same toxins that produce SSSS; however, bullous impetigo results in only a localized release of the exfoliative exotoxin. Bullous lesions such as bullous pemphigoid and pemphigus vulgaris should also be considered. A dermatology consult is recommended for prompt and accurate diagnosis.

The treatment of SSSS typically requires hospitalization and relies heavily on supportive measures including aggressive fluid resuscitation and meticulous wound care. In general, SSSS cases not associated with MRSA are treated with penicillinase-resistant antistaphylococcal antibiotics such as nafcillin or oxacillin. In MRSA-associated SSSS cases, vancomycin is often used. Though the use of petroleum-based gauze to prevent further epidermal damage may be necessary; the number of dressing changes should be minimized due to the fragile nature of the skin and blisters should be left intact. Comfort measures should include the use of pressure-relieving mattresses and adequate analgesia. In severe cases of SSSS, patients may require ICU admission and care similar to burn victims. Corticosteroids are contraindicated in the treatment of SSSS because they have the potential to worsen an existing immunocompromised state.[6]

Children affected by SSSS typically recover fully in only one to two weeks; however, adults often experience complications such as cellulitis, pneumonia, electrolyte disturbances, and even death. Most adult patients affected by SSSS have underlying irreversible co-morbidities and depressed immune status, which contribute to a very high mortality rate. In childhood-associated SSSS the mortality rate is less than 4%, but in adults it is reported to be greater than 60%.[5]

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CME QUESTIONS

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For each question, choose the one answer that is most correct.

1. True or False:
   Staphylococcal Scalded Skin Syndrome (SSSS) is much more commonly described in adults than children.

2. All of the following are true except:
   a. SSSS is a toxin-mediated exfoliative dermatitis.
   b. Nikolsky's sign is not a characteristic feature of SSSS.
   c. Mucous membranes are not involved in SSSS.
   d. Adults that are vulnerable to SSSS are typically immunocompromised.

3. True or False:
   The mortality rate for SSSS in children is reportedly much greater than in adults.

4. Which one of the following statements is false:
   a. Skin biospy of affected areas in SSSS reveal subcorneal splitting along the stratum granulosum without dermal infiltration, bacterial organisms, or inflammatory cells.
   b. The differential diagnosis of SSSS includes drug hypersensitivity reactions, scarlet fever and viral-associated exanthems.
   c. Unlike SSSS, TEN involves mucous membranes.
   d. Pain is not a characteristic feature of the rash of SSSS.

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