A Deadly Threat of Staphyloccus: A Rare Case of Staphylococcal Skin Scalded Syndrome with Toxic Shock Syndrome

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Submission date: 12-Aug-2025 03:15PM (UTC+0700)
Submission ID: 2690338851
File name: IJAR-53257.docx (368.05K)
Word count: 1775
Character count: 10408

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Abstract:
Staphylococcal scalded skin syndrome (SSSS), also known as Ritter disease or neonatal pemphigus, is a rare exfoliating skin disease caused due to exfoliative toxin of *Staphylococcus aureus*. It primarily affects infants and younger children. Staphylococcal toxic shock syndrome (STSS) is an acute life-threatening multisystem illness also caused by toxigenic strains of *Staphylococcus aureus*.
An 8 years old girl child was admitted to ICU in altered sensorium. She had history of high-grade fever with chills, diarrhoea, oliguria and generalized exfoliative erythematous skin rashes. She had abscess over the left arm following a tetanus toxoid injection given 2 weeks prior for a minor injury. On physical examination, child was pale and icteric. She had clinical features of shock with markedly deranged laboratory parameters including TLC, renal & liver enzymes, coagulation profile and electrolytes. Immediate supportive management was provided and empirical antibiotics started. Pus was drained from left arm abscess which showed growth of Methicillin resistant *Staphylococcus aureus* (MRSA). Blood culture was negative. A working diagnosis of Staphylococcal scalded skin syndrome with toxic shock syndrome was made. Patient responded well to antibiotics vancomycin & clindamycin, and other symptomatic management.
SSSS with STSS is an acute emergency with multisystem involvement. A clinical suspicion with prompt diagnosis on the basis of clinical spectrum and microbiology reports can be life saving for the patient.

Keywords: *Staphylococcus aureus*, Nikolsky sign, Exfoliative toxin, Scalded skin, toxic shock syndrome, superantigen

Introduction:

Staphylococcal scalded skin syndrome (SSSS) and toxic shock syndrome (STSS), both are rare illnesses caused by toxigenic strains of *S. aureus*. SSSS, also known as Ritter disease or neonatal pemphigus, is a rare superficial exfoliating skin disorder. On the other hand, STSS is an acute life-threatening multisystem illness.[1,2] The bacteria from locally colonized sites such as the upper respiratory tract, ears, eyes, abscesses, fistulas, or joint infections release toxins at the primary infection site which is located away from the skin denuded areas. SSSS primarily affects infants and younger children but may affect adults with renal malfunction or immunological deficiency.[3] Multiple blistering skin disorders like Stevens-Johnson syndrome (SJS), epidermolysis bullosa, and toxic epidermal necrolysis (TEN) may mimic the condition.[4] Hence, a thorough history taking and clinical examination is crucial to make the accurate diagnosis. Here, we present a rare case of staphylococcal scalded skin syndrome with toxic shock syndrome.

Case presentation:

An 8-year-old girl from Gorakhpur sustained a minor forehead injury and received a tetanus toxoid injection. Two days later, she developed swelling and pain at the injection site, followed by vomiting, high-grade fever with chills, diarrhea, reduced urine output, and confusion. She was initially managed at a private hospital where labs revealed deranged liver and renal parameters. Due to worsening symptoms, she was referred to a higher center.
On arrival, she was in altered sensorium, febrile, pale, icteric, and appeared toxic. General examination revealed facial puffiness, pedal edema, subconjunctival hemorrhages, and oral

ulcers. A 5×5 cm tender, warm, red swelling with a yellow center was noted over the left deltoid region. Generalized erythematous, desquamating rashes were present over the entire body, including scalp and genitalia, with a positive Nikolsky's sign (Fig 1).
There was no relevant medical or family history. Systemic examination revealed abdominal distension and epigastric tenderness, but no organomegaly or focal neurological findings.
Routine blood investigations were done at the time of admission as shown in table I. Pus culture from the arm abscess showed Methicillin resistant *Staphylococcus aureus* (MRSA) growth, sensitive to vancomycin, amikacin, and teicoplanin. Blood and urine cultures were sterile. Viral and tropical disease panels were negative.
She was admitted to the ICU and treated with IV vancomycin and clindamycin, along with supportive care including oxygen, fluids, inotropes, and wound management. Skin lesions began healing by day 4, and she was discharged in stable condition after 10 days.

Discussion:

SSSS is a rare superficial skin disorder that varies from local blistering to generalised scalding leading to marked hypothermia and hemodynamic instability.[5] This condition is named Ritter disease in 1878 after German physicist Baron Gotfried Ritter von Rittershain published a series of 297 cases in young children.[4]

It typically occurs following colonization with exfoliative toxin (ETA and ETB) producing *S. aureus*. Staphylococci phage group 2, particularly strains 55 and 71, are the most commonly implicated strains in SSSS.[1] The disease usually follows a localized infection from the upper respiratory tract, ears, conjunctiva, or umbilical stump. In adults, it may result from an abscess, arteriovenous fistula infection, or septic arthritis. In present case, a skin abscess following an injection acted as nidus for infection.[3]

The toxins likely act as serine proteases that target the protein desmoglein -1 (dsg1) which is a transmembrane desmosomal glycoprotein crucial for the maintenance of interkeratinocyte adhesion. Exotoxin causes separation of epidermis beneath the granular cell layer resulting in typical skin lesions. Skin biopsy demonstrate a split in granular layer with inflammatory cell infiltrate.[1,4]

There are 2 clinical variants of SSSS: localized and generalized. Localized form, also known as bullous impetigo, involves flexures like axilla, groin and limb flexures. Generalized SSSS involves whole body causing generalized scalding and detachment of skin following mere rubbing (Nikolsky sign).[1,3]

TSS is a toxin mediated acute life threatening illness caused by *S. aureus*. It was first described in a pediatric case series in 1978. In early 1980s, high absorbency tampon use in menstruating women led to an alarming rise in cases of TSS. Later on, several cases of TSS were reported from men and non menstruating women indicating its multiple pathogenic mechanisms.[6]

The enterotoxin and toxin-1 released by *S. aureus* act as superantigens leading to non specific T cell activation causing massive release of cytokines. Patient present with fever and non-specific symptoms rapidly worsening to multisystem organ failure and toxic shock. Hypotension, shock, respiratory paralysis, renal and hepatic failure may occur due to TNF-alpha and interleukins.[7]

Age of the child, typical skin lesions with desquamation and positive nikolsky's sign led to the diagnosis of SSSS. The present case also fulfills the diagnostic criteria – both clinical as well as laboratory, for TSS given by Centers for Disease Control and Prevention, 2011. Clinical criteria includes fever, diffuse macular erythematous rash with desquamation, hypotension (< 5th percentile of age for children) and multisystem involvement (≥3 of following organ systems: gastrointestinal, muscular, mucous membrane, renal, hepatic, hematological and central nervous system). Laboratory criteria includes negative blood or cerebrospinal fluid cultures and negative serology for Rocky Mountain spotted fever, leptospirosis, or measles.[8] Hence, the case was diagnosed to have SSSS with STSS.

Diagnosis in both the scenarios is clinical in majority of the cases. *S. aureus* is rarely isolated from the blood cultures as the disease is toxin mediated. Cultures from primary infection site are usually positive as in present case. Confirmation of diagnosis can be done by detection of causative toxins using PCR.[2,4]

Both SSSS and TSS can be managed by timely administration of antistaphylococcal antibiotics. If MRSA is suspected, vancomycin or linezolid are the drug of choice. Treatment with clindamycin and linezolid is preferred as they can neutralise the toxin production. However, linezolid should be used with caution as it may aggravate the thrombocytopenia.[2,4] This case was treated with vancomycin and clindamycin.

Although, both SSSS and STSS are toxin mediated illnesses caused by different strains of *S. aureus*, they rarely exist together. To the best of our knowledge, this is the 3rd case of concurrent SSSS and STSS reported till date.[9,10] First case was reported in Japan in an adult with liver cirrhosis.[9] Second reported case occurred in a 43 years old man following a tooth extraction.[10] In this case, the causative toxins could not be identified due to unavailability of molecular tests. However, detection of *S. aureus* from skin abscess and negative blood cultures helped in concluding the diagnosis.

Conclusion: Although rare, a possibility of 2 toxin mediated illnesses, SSSS and TSS, by S. *aureus* should be kept in mind in patients presenting with fever and acute generalized exfoliative erythroderma with multisystem involvement or shock. It is crucial to detect the primary focus of pathogenic organism to curb the root cause of illness and differentiating it from other causes of blistering skin disorders. A prompt diagnosis and timely management with effective antibiotics can be life saving for the patient.

Acknowledgement: None

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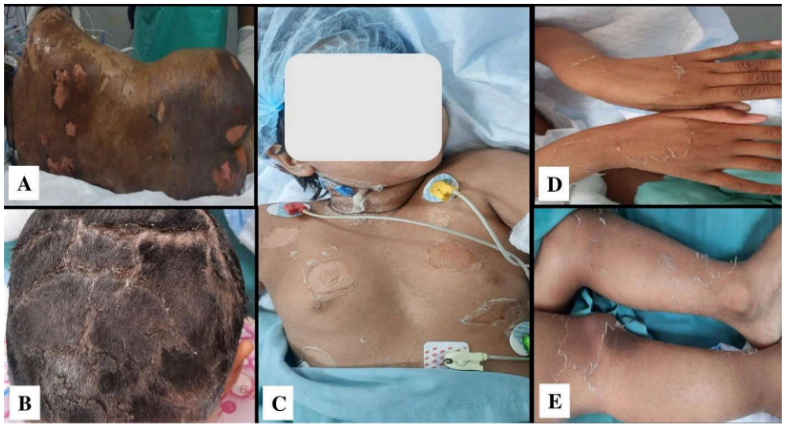
Table I: Routine blood investigations of the patient at the time of admission

Parameter	Result	Normal range
Hemoglobin	9.3 g/dl	12.3-16.2 g/dl
Total leucocyte count	25,000/µl	4,000-11,000/µl
Platelet count	64 X 1000/ µl	150-400 X 1000/µl
Erythrocyte sedimentation rate	39 mm/hr	0-20 mm/hr
Serum Creatinine	3.3 mg/dl	0.6-1.5 mg/dl
Blood urea nitrogen	69 mg/dl	7-20 mg/dl
Total bilirubin	4.8 mg/dl	0.2-1.2 mg/dl
Conjugated bilirubin	2.1 mg/dl	0.1-0.3 mg/dl
Aspartate aminotransferase	89 U/L	5-40 U/L
Alanine aminotransferase	60 U/L	5-40 U/L
Serum albumin	2.5 g/dl	3.8-5.5 g/dl
Serum amylase	1834 U/L	11-90 U/L
Prothrombin time	16.5 sec	13.5 sec

Fig 1: Extensive erythematous exfoliative skin lesions over the back and hip region (A) and scalp (B). Healed exfoliated lesions over chest (C), dorsum of wrist and hands (D) and lower limbs (E)


A
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