Hilla University College Journal For Medical Science

Manuscript 1048

Staphylococcal Scalded Skin Syndrome (SSSS): A Short Review

Anmar M. K. Al-Maamori

Zahraa M. Altaee

Noor Mahommoud Naj

Rafflaa S. Hussien

REVIEW

Hilla Univ Coll J Med Sci

Staphylococcal Scalded Skin Syndrome (SSSS): A Short Review

Anmar M. K. Al-Maamori, Zahraa M. Altaee *, Noor Mahommoud Naj, Rafflaa S. Hussien

Department of Biology, College of Science, University of Babylon, Hilla, Iraq

Abstract

Staphylococcal scalded skin syndrome (SSSS) is a skin problem characterized by the formation of blisters. It primarily affects newborns, young children, and adults with pre-existing medical conditions. This condition is caused by an infection from the bacteria *Staphylococcus aureus*. The cause of this case is the breakdown of desmoglein-1, a protein in the skin, due to the action of exotoxins. This results in the outer layer of the skin's cells peeling off. The SSSS is caused by the dissemination of toxins throughout the body, leading to a widespread rash and a severe manifestation of symptoms. Staphylococcal scalded skin syndrome manifests as the formation of blisters on the outermost layers of the skin, caused by the release of exfoliative toxins from *S. aureus*. Erythematous cellulitis develops with the rapid exfoliation of skin cells. A sign of SSSS is a small number of blisters restricted to the infection site that progress to widespread exfoliation that affects the entire body. The condition is managed using antibiotics that specifically target S. aureus. This illness may occasionally be mistaken for other conditions that cause superficial blistering.

Keywords: Staphylococcal scalded skin (SSS) syndrome, *S. aureus*, Exfoliative toxins (ETs)

1. Introduction

Staphylococcal scalded skin syndrome (SSSS), commonly referred to as Ritter disease, is a potentially fatal infection brought on by specific strains of S. aureus that produce exfoliative toxins. From a clinical perspective, this condition is defined by the removal of the skin's outer layer, resulting in the appearance of significant surface blisters that resemble skin burned by hot liquid [1]. The prevalence of SSSS in the general population ranges from 0.09 to 0.56 instances per one million individuals [2]. Nevertheless, SSSS is predominantly observed in kids aged six and below [3]. The higher occurrence in young children can be attributed to their insufficient production of antibodies that defend against exfoliative toxins and their reduced ability to eliminate these toxins from the body due to their underdeveloped renal function [4]. The rate of mortality that occurs as a result of infection with SSSS is below 5% in children and above 60% in adults, possibly related to an underlying immunodeficiency or comorbidities [2–4].

Antibodies that specifically target exotoxins and enhanced elimination of exotoxins reduce the occurrence of SSSS in adults. This condition is characterized by the shedding of the skin's outermost layer, followed by a sudden inflammation of the skin known as acute erythematous cellulitis [5]. The severity of SSSS ranges from minor blisters of watery on certain areas of the skin to extensive ex-foliation that impacts the entire surface of the body. The presence of blisters that red color on the surface of the skin that appears burned or scaled is indicative of a condition known as staphylococcal scalded skin syndrome [6]. Staphylococcus aureus strains that generate toxins are capable of releasing two specific exotoxins known as epidermolysis toxins A and B. The toxins are the fundamental components of SSSS infection

Received 29 September 2024; accepted 19 March 2025.
Available online 2 May 2025

* Corresponding author.
E-mail addresses: sci.anmar.mahdi@uobabylon.edu.iq (A. M. K. Al-Maamori), sci.azhar.omran@uobabylon.edu.iq (Z. M. Altaee), sci.noor.mahmood@uobabylon.edu.iq (N. M. Naj), sci.raflaa.sabek@uobabylon.edu.iq (R. S. Hussien).

https://doi.org/10.62445/2958-4515.1048

[7, 8]. Desmosomes, which are essential components of the skin, function to bind to neighboring skin cells. The toxins produced by *S. aureus* attach to the molecule Desmoglein 1, which is located within the desmosome. This interaction causes the skin cells to lose their ability to stick together, resulting in a loss of adherence [9].

2. Toxins of *Staphylococcus aureus*

S. aureus is a Gram-positive bacteria that appears purple when stained with the Gram stain. It has a spherical shape and prefers to form clusters resembling grapes. These organisms have the ability to thrive in environments with salt concentrations of up to 10%. Their colonies typically exhibit a golden or yellow coloration. They are catalase-positive, which is a characteristic shared by all pathogenic *Staphylococcus* species. Additionally, they are coagulase-positive, a trait that helps differentiate Staphylococcus aureus from other Staphylococcus species. Lastly, they are mannitol fermentation positive, a feature that aids in distinguishing them from Staphylococcus epidermidis. Staphylococcus aureus secretes a multitude of toxins and enzymes that have the potential to inflict severe harm on tissues and organs, resulting in skin infections characterized by blisters, lung infections, and instances of food poisoning, among other manifestations [10]. Certain strains of this pathogens commonly induce infections by producing toxins and utilizing certain surface proteins that, upon binding, result in the inactivation of antibodies. *S. aureus* strains release many exotoxins [9].

The primary toxins produced by *S. aureus* can be categorized into three main groups: 1)pore-forming toxins (PFTs), 2)exfoliative toxins (ETs), and 3)superantigens (SAgs). Pore-forming toxins can be categorized into four distinct types: 1) Hemolysin-α (Hla or α-toxin), 2) Hemolysin-β, 3) leukotoxins, and 4) phenol-soluble modulins (PSMs) [11].

These toxins are associated with many illnesses including staphylococcal scalded skin syndrome, necrotizing pneumonia, toxic shock syndrome (TSS), and deep-seated skin infections [8, 12–15]. The toxins have the ability to harm the cell membranes of the host, either by breaking down inter-cellular connections or by altering immunological responses [11].

3. Exfoliative toxins (ETs)

Exfoliative toxins (ETs), often referred to as epidermolysis toxins, are produced by staphylococci and play a crucial role in causing the staphylococcal scalded skin condition. These toxins are considered virulence factors. Exfoliative toxins are a sort of serine proteases that have a high level of specificity for their target and are able to break down a specific peptide bond in the extracellular part of desmoglein 1 (Dsg1), which is a form of cell-cell adhesion protein called a desmosomal cadherin. The process of hydrolysis leads to the separation of keratinocytes in both animal and human skin [17, 18].

The Exfoliative toxins (ETs) possess a three-dimensional configuration that closely resembles that of glutamate-specific serine proteases. They consist of a catalytic triad made up of serine, histidine, and aspartate which forms the active site, and two substrate-binding domains. However, in contrast to conventional serine proteases, the exfoliative toxins have a highly charged N-terminal alpha-helix and a distinct arrangement of a crucial peptide bond. This arrangement obstructs the active site of the toxins, preventing them from exhibiting any significant enzymatic activity in their natural state. The identified target for the toxins is desmoglein-1, a glycoprotein found in the superficial epidermis that is crucial for sustaining cell-to-cell contact through desmosomes. The speculation is that when the N-terminals alpha-helix binds to des-moglein-1, it causes a altration in shape that opens the toxin's active site. This allows the toxin to split the extracellular area of des-moglein-1 between the third and fourth domains. As a result, intercellular adhesion is disrupted and superficial blisters form.

Von Rittershain documented the clinical characteristics of epidermal ex-foliation in newborns in 1878 [15]. Nevertheless, the correlation between exfoliation and S. aureus was first identified in 1967 by Lyell. The delay in the discovery of Ritter and Lyell was due to the absence of cultivable staphylococci in the blister fluid and exfoliated regions. This is because the toxin is spread from remote infection sites into the bloodstream. In 1972, Melish *et al*. identified a theoretical toxin, earlier proposed by Lyell, and provided evidence of its harmful effect in newborn mice, which were utilized as experimental subjects [20, 21].

ETs, or exotoxins, are substances that cause the separation of keratinocyte junctions and cell-cell adhesion in the host's epidermis. This process leads to the peeling of the skin and the production of blisters (Fig. 1). So far, researchers have discovered three distinct ET serotypes (ETA, ETB, and ETD) in *S. aureus*. These serotypes feature amino acid sequences that resemble trypsin-like serine proteases. They have been linked to staphylococcal skin infections, including SSSS or bullous impetigo, in humans [17].

3.1. Symptoms on skin

Exfoliative toxin Staphylococcal scalded-skin syndrome, often recognized as SSSS, is a condition

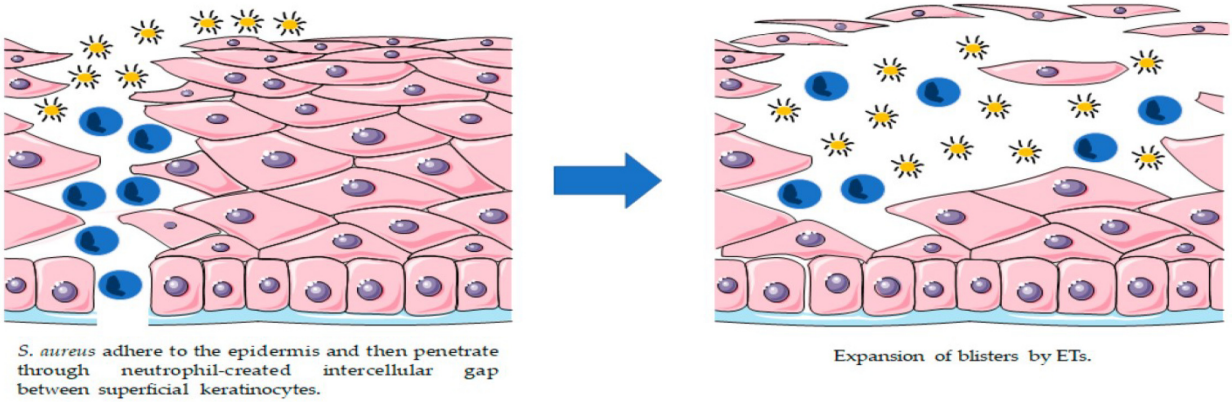

Fig. 1. The blistering caused by extracellular toxins (ETs) of staphylococcal bacterial invasion [21].

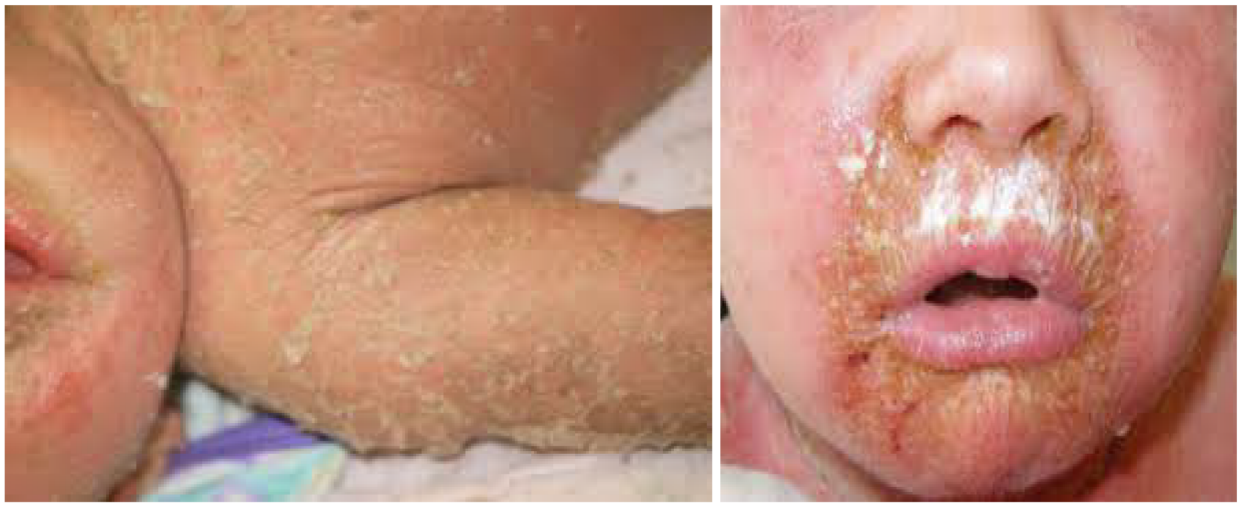

Fig. 2. Staphylococcal scalded skin syndrome [28].

characterized by the formation of blisters on the skin surface, caused by the release of a toxin from Staphylococcus aureus bacteria. The toxin induces detachment of cells in the epidermis. The text is enclosed in tags. The primary manifestation of SSSS is the separation of the outermost layer of the skin. The exfoliative toxin targets Desmoglobin, a protein responsible for cellular adhesion, resulting in superficial lesions in the groin, armpits, nose, and ears. These lesions appear as fluid-filled blisters resembling tissue paper. The skin rashes proliferate swiftly to additional limbs and torsos. Newborns frequently develop skin rashes related to SSSS in the diaper region. Following a 24-hour period of infection, the outer layer of the skin is detached in small sections, resulting in a damp and reddened region on the surface (Fig. 2). Additional symptoms of SSSS encompass severe pain localized at the site of infection, muscular weakness, exhaustion, and excessive loss of bodily fluids [23–25].

3.2. *Identification of SSS*

The skin's appearance unequivocally exhibits indications of SSSS. The exudate or purulent discharge collected on a cotton swab is utilized for the detection of staphylococcal bacteria. In certain instances, a blood test is used to verify the presence of the infection. A little skin sample is often sent for microscopic analysis [2].

SSSS is predominantly diagnosed through clinical assessment. However, if the clinical presentation is uncertain, if the response to treatment is inadequate, or if there is an occurrence of skin infections caused by *S. aureus* can be verified using histological and molecular testing [26].

4. Treatment/management

Early administration of antibiotics that target staphylococcus is recommended, specifically

Cifazolin, Nafcellin, or Oxacillin for *S. aureus* that is methicillin-sensitive (MSSA). Vancomycin must be given in cases where there is suspicion of methecillin-resistant Staphylococcus aureus (MRSA), particularly in individuals who have recently been exposed to healthcare facilities or in regions with a high occurrence of MRSA. Topical antibiotics alone are insufficient, and even in cases with localized Staphylococcal Scalded Skin Syndrome, treatment with systemic antibiotics is necessary. If there is a concern about a subsequent bacterial skin infection, it is recommended to begin extra antibiotics that can effectively treat *Pseudomonas* bacteria. Individuals displaying symptoms of dehydration and/or sepsis should receive intravenous (IV) fluids [27, 28].

To facilitate healing and minimize heat loss, it is recommended to apply emollient and non-adherent dressings to the skin and areas that are lacking protective covering. Providing supportive care, which involves addressing dehydration, regulating body temperature, and ensuring proper nourishment, is extremely crucial. Patients with extensive skin involvement are susceptible to hypothermia and dehydration as a result of epidermal loss. Avoid using silver sulfadiazine due to its propensity to be absorbed into the body and cause toxicity [29].

If severe cases arise, it is advisable to consider admitting the patient to a burn unit, if available. Persons diagnosed with Staphylococcal Scalded Skin Syndrome must be placed in isolation to limit the risk of infectious and outbreaks. Practicing hygiene of hand while implementing contact isolation measures and ensuring thorough washing of devices, stethoscopes, for example, is crucial to preventing the spread of this disease in hospitals. It is essential to identify and treat individuals who have the potential to carry toxin-producing strains of Staphylococcus aureus in order to avert epidemics. It is recommended that those who are taking care of the patient should test for *S. aureus* using a nasal swab and receive treatment if the test is positive [1].

5. Conclusion

Staphylococcal scalded skin syndrome (SSSS) is a severe condition characterized by the rapid shedding of the skin, accompanied by inflammation of the skin known as erythematous cellulitis. The primary factor responsible for this phenomenon is the exfoliative toxins produced by *S. aureus.* The majority of SSSS cases can be completely cured, particularly when treatment is initiated during the early stages of the condition. After achieving full recovery, no noticeable discrepancies or enduring blemishes manifest on the skin's surface. SSSS is managed by systemic administration of oral antibiotics, which may be administered intravenously in acute cases. The skin must be cleansed and treated with antiseptic materials, immediate medical intervention is necessary in cases of fluid or electrolyte imbalance.

Ethical issue

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of University of Babylon collage of Sciences (Date1-10-2024/No B241002).

Financial funding

This research received no external funding.

Conflicts of interest

The authors declare no conflict of interest.

References

1. Liy-Wong C, Pope E, Weinstein M, Lara-Corrales I. Staphylococcal scalded skin syndrome: An epidemiological and clinical review of 84 cases. Pediatr Dermatol [Internet]. 2021;38(1):149–53. Available from: http://dx.doi.org/10.1111/pde.14470.
2. Handler MZ, Schwartz RA. Staphylococcal scalded skin syndrome: diagnosis and management in children and adults. J Eur Acad Dermatol Venereol [Internet]. 2014;28(11):1418–23. Available from: http://dx.doi.org/10.1111/jdv.12541.
3. Ross A, Shoff HW. Staphylococcal scalded skin syndrome. In *StatPearls. Treasure Island (FL): StatPearls Publishing*; 2024.
4. Leung AKC, Barankin B, Leong KF. Staphylococcal-scalded skin syndrome: Evaluation, diagnosis, and management. *World J Pediatr [Internet]*. 2018;14(2):116–20. Available from: http://dx.doi.org/10.1007/s12519-018-0150-x.
5. Sah P, Rijal KR, Shakya B, Tiwari BR, Ghimire P. Nasal carriage rate of staphylococcus aureus in hospital personnel of national medical college and teaching hospital and their susceptibility pattern. *J Health Appl Sci*. 2013;3:21–3.
6. Farroha A, Frew Q, Jabir S, Dziewulski P. Staphylococcal scalded skin syndrome due to burn wound infection. *Ann Burns Fire Disasters*. 2012;25(3):140–2.
7. Hanakawa Y, Stanley JR. Mechanisms of blister formation by staphylococcal toxins. *J Biochem [Internet]*. 2004;136(6):747–50. Available from: http://dx.doi.org/10.1093/jb/mvh182.
8. Ladhani S. Understanding the mechanism of action of the exfoliative toxins of staphylococcus aureus. *FEMS Immunol Med Microbiol [Internet]*. 2003;39(2):181–9. Available from: http://dx.doi.org/10.1016/S0928-8244(03)00225-6.
9. Hubiche T, Bes M, Roudiere L, Langlaude F, Etienne J, Del Giudice P. Mild staphylococcal scalded skin syndrome: An underdiagnosed clinical disorder: Correspondence. *Br J Dermatol [Internet]*. 2012;166(1):213–5. Available from: http://dx.doi.org/10.1111/j.1365-2133.2011.10515.x.
10. Rasigade J-P, Vandenesch F. Staphylococcus aureus: A pathogen with still unresolved issues. *Infect Genet Evol [Internet]*. 2014;21:510–4. Available from: http://dx.doi.org/10.1016/j.meegid.2013.08.018.
11. Grumann D, Nübel U, Bröker BM. Staphylococcus aureus toxins – their functions and genetics. *Infect Genet Evol [Internet]*. 2014;21:583–92. Available from: http://dx.doi.org/10.1016/j.meegid.2013.03.013.

12. Dinges MM, Orwin PM, Schlievert PM. Exotoxins of staphylococcus aureus. *Clin Microbiol Rev [Internet]*. 2000;13(1):16–34. Available from: http://dx.doi.org/10.1128/cmr.13.1.16-34.2000.
13. Abbas EC, Al-mohana, AM, Al-Dhalimi MA, Al-Charrakh AH. Cytokine serum level association with superantigen production by *Staphylococcus aureus* in psoriasis vulgaris. *Research Journal of Pharmaceutical, Biological and Chemical Sciences*. 2016;7(4):172–180.
14. Jarraud S, Cozon G, Vandenesch F, Bes M, Etienne J, Lina G. Involvement of enterotoxins G and I in staphylococcal toxic shock syndrome and staphylococcal scarlet fever. *J Clin Microbiol [Internet]*. 1999;37(8):2446–9. Available from: http://dx.doi.org/10.1128/JCM.37.8.2446-2449.1999.
15. Jarraud S, Mougel C, Thioulouse J, Lina G, Meugnier H, Forey F, *et al.* Relationships between *Staphylococcus aureus* genetic background, virulence factors, *agr* groups (alleles), and human disease. *Infect Immun [Internet]*. 2002;70(2):631–41. Available from: http://dx.doi.org/10.1128/iai.70.2.631-641.2002.
16. Seilie ES, Bubeck Wardenburg J. *Staphylococcus aureus* pore-forming toxins: The interface of pathogen and host complexity. *Semin Cell Dev Biol [Internet]*. 2017;72:101–16. Available from: http://dx.doi.org/10.1016/j.semcdb.2017.04.003.
17. Mariutti RB, Tartaglia NR, Seyffert N, Castro TL de P, Arni RK, Azevedo VA, *et al.* Exfoliative toxins of staphylococcus aureus. In *The Rise of Virulence and Antibiotic Resistance in Staphylococcus aureus*. InTech; 2017.
18. Ladhani S. Understanding the mechanism of action of the exfoliative toxins of*Staphylococcus aureus*. *FEMS Immunol Med Microbiol [Internet]*. 2003;39(2):181–9. Available from: http://dx.doi.org/10.1016/s0928-8244(03)00225-6.
19. Ladhani S, Garbash M. Staphylococcal skin infections in children: Rational drug therapy recommendations. *Paediatr Drugs [Internet]*. 2005;7(2):77–102. Available from: http://dx.doi.org/10.2165/00148581-200507020-00002.
20. Oliveira D, Borges A, Simões M. Staphylococcus aureus toxins and their molecular activity in infectious diseases. *Toxins (Basel) [Internet]*. 2018;10(6). Available from: http://dx.doi.org/10.3390/toxins10060252.
21. Krieg T, Bickers DR, Miyachi Y. *Therapy of skin diseases: A worldwide perspective on therapeutic approaches and their molecular basis*. London, New York; Heidelberg Dordrecht: Springer; 2010.
22. Hanakawa Y, Schechter NM, Lin C, Garza L, Li H, Yamaguchi T, *et al.* Molecular mechanisms of blister formation in bullous impetigo and staphylococcal scalded skin syndrome. *J Clin Invest [Internet]*. 2002;110(1):53–60. Available from: http://dx.doi.org/10.1172/jci0215766.
23. Mishra AK, Yadav P, Mishra A. A systemic review on staphylococcal scalded skin syndrome (SSSS): A rare and critical disease of neonates. *Open Microbiol J [Internet]*. 2016;10(1):150–9. Available from: http://dx.doi.org/10.2174/1874285801610010150.
24. Nusman CM, Blokhuis C, Pajkrt D, Visser DH. Staphylococcal scalded skin syndrome in neonates: Case series and overview of outbreaks. *Antibiotics (Basel) [Internet]*. 2022;12(1):38. Available from: http://dx.doi.org/10.3390/antibiotics12010038.
25. Braunstein I, Wanat KA, Abuabara K, McGowan KL, Yan AC, Treat JR. Antibiotic sensitivity and resistance patterns in pediatric staphylococcal scalded skin syndrome. *Pediatr Dermatol [Internet]*. 2014;31(3):305–8. Available from: http://dx.doi.org/10.1111/pde.12195.
26. Ladhani S, Joannou CL, Lochrie DP, Evans RW, Poston SM. Clinical, microbial, and biochemical aspects of the exfoliative toxins causing staphylococcal scalded-skin syndrome. *Clin Microbiol Rev [Internet]*. 1999;12(2):224–42. Available from: http://dx.doi.org/10.1128/cmr.12.2.224.
27. Baartmans MGA, Dokter J, den Hollander JC, Kroon AA, Oranje AP. Use of skin substitute dressings in the treatment of staphylococcal scalded skin syndrome in neonates and young infants. *Neonatology [Internet]*. 2011;100(1):9–13. Available from: http://dx.doi.org/10.1159/000317997.
28. Ruszkowska L, Dziekan G, Olechowska M. Staphylococcal scalded skin syndrome in six children. *Dermatology Review/Przegląd Dermatologiczny*. 2009;96(4):279–284.
29. Al-Zaidi, JR. Methicillin Resistant Staphylococcus aureus (MRSA) nasal carriage among health care workers in intensive care units. *Med J Babylon*. 2014;11(3):749–57.