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Clinical Review

THE EVALUATION AND MANAGEMENT OF TOXIC SHOCK SYNDROME IN THE EMERGENCY DEPARTMENT: A REVIEW OF THE LITERATURE

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☐ **Abstract—Background: Toxic shock syndrome (TSS) is a severe, toxin-mediated illness that can mimic several other diseases and is lethal if not recognized and treated appropriately. Objective: This review provides an emergency medicine evidence-based summary of the current evaluation and treatment of TSS. Discussion: The most common etiologic agents are *Staphylococcus aureus* and *Streptococcus pyogenes*. Sources of TSS include postsurgical wounds, postpartum, postabortion, burns, soft tissue injuries, pharyngitis, and focal infections. Symptoms are due to toxin production and infection focus. Early symptoms include fever, chills, malaise, rash, vomiting, diarrhea, and hypotension. Diffuse erythema and desquamation may occur later in the disease course. Laboratory assessment may demonstrate anemia, thrombocytopenia, elevated liver enzymes, and abnormal coagulation studies. Diagnostic criteria are available to facilitate the diagnosis, but they should not be relied on for definitive diagnosis. Rather, specific situations should trigger consideration of this disease process. Treatment involves intravenous fluids, source control, and antibiotics. Antibiotics should include a penicillinase-resistant penicillin, cephalosporin, or vancomycin (in methicillin-resistant *S. aureus* prevalent areas) along with either clindamycin or linezolid. Conclusion: TSS is a potentially deadly disease requiring prompt recognition and treatment. Focused history, physical examination, and laboratory testing are important for the diagnosis and management of this disease. Understanding the evaluation and treatment of TSS can assist providers with effectively managing these patients. Published by Elsevier Inc.**

☐ **Keywords—infection; toxic shock syndrome; *Staphylococcus aureus*; *Streptococcus pyogenes*; toxin; fever; hypotension; rash; erythroderma; desquamation**

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INTRODUCTION

Toxic shock syndrome (TSS) is an acute, toxin-mediated illness characterized by fever, hypotension, multi-organ dysfunction, and a diffuse rash with desquamation (1). The disease can be rapidly lethal and is usually treatable, though physicians often fail to recognize this condition. The annual incidence has been suggested to range from 1.5–11 per 100,000 people (1–10). Cases occur most commonly at the extremes of age, with one study finding that the highest incidence occurred in adults aged > 45 years, followed by children < 5 years, and was lowest in persons aged 16–45 years (5). Another study found higher rates among children < 2 years of age and adults ≥ 65 years of age (6). TSS is more commonly seen in winter and spring, with a lower incidence in summer and autumn months (6–12).

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Although TSS is most commonly associated with *Staphylococcus aureus* and *Streptococcus pyogenes*, several other infections have also been associated with this illness, including *Streptococcus agalactiae*, *Streptococcus viridans*, Group C *Streptococcus*, Group G *Streptococcus*, and *Clostridium soredellii* (13–21). Staphylococcal TSS was first described in 1978 in association with an *S. aureus* infection in children, followed by an epidemic in the 1980s, occurring in association with tampon use (1,22,23). However, changes in the manufacturing and use of tampons led to a significant decline in the incidence of menstrual-related staphylococcal TSS, whereas the incidence of nonmenstrual staphylococcal TSS has increased (1,24,25). Nonmenstrual staphylococcal TSS has been associated with postsurgical, postpartum, postabortion, intrauterine device placement, burns, soft tissue injuries, and focal infections (e.g., pneumonia, influenza) (1,10,21,26–37).

Streptococcal TSS occurs more commonly after viral infections (e.g., varicella, influenza), pharyngitis, and local soft tissue trauma (1,10,26,38–41). Streptococcal TSS is associated with deeper sites of infection (e.g., infection after penetrating injuries, necrotizing fasciitis) and has higher rates of morbidity and mortality than staphylococcal TSS (1). Overall TSS mortality for adults ranges from 30–80% for TSS, whereas mortality in children is much lower and ranges from 3–10% (1,9,10,25,42).

METHODS

Authors searched PubMed and Google Scholar for articles using the keyword "toxic shock syndrome." The literature search was restricted to studies published in English. Authors decided which studies to include for the review by consensus. A total of 112 articles were selected for inclusion in this review.

DISCUSSION

Pathogenesis

TSS is caused by a host response to superantigens from the associated bacteria (commonly *S. aureus* or *S. pyogenes*) (1,43–49). Superantigens are a group of proteins that can directly activate T cells by bypassing certain steps of the antigen-mediated immune response sequence (1,43,44,46,47,49). This causes a massive, uncontrolled T-cell activation, resulting in the release of a substantial amount of cytokines (1,43,44,46–49). This leads to recruitment and further activation of additional T and B cells (1,43,44,46,47,49). The massive cytokine release is believed to be responsible for the most severe features of TSS (1,43–49).

Antibodies against these superantigens significantly lowers one's risk of developing TSS (1,50,51). The prevalence of antibodies against toxic shock syndrome toxin 1 (TSST-1), one of the primary superantigens associated with staphylococcal TSS, is over 90% in the adult population, but much lower in the pediatric population (1,52–54). It was hypothesized that most patients acquired the antibody due to mucosal colonization with TSST-1 producing *S. aureus*, because most of the adults had never developed TSS (1,53,54). Similar benefits have been found among patients with antibodies against other streptococcal superantigens, whereas an inability to produce anti-TSST-1 antibodies after an episode of staphylococcal TSS predisposes patients to recurrent episodes (1,55,56).

History and Physical Examination

Patients with TSS often present with a combination of symptoms due to two factors: toxin secretion and the infection focus. Disease manifestations include fever, hypotension, and skin changes (39,57–59). Other symptoms can include chills, generalized weakness, malaise, headache, sore throat, vomiting, diarrhea, abdominal pain, and lightheadedness (23,39,56–61). These symptoms may resemble a viral illness, such as influenza, early in the disease state (62–65). Myalgias and generalized weakness are typically the first symptoms, along with diarrhea, sore throat, and headache. Symptoms can then progress rapidly, especially in otherwise healthy patients, with diffuse erythroderma, watery diarrhea, oliguria, and extremity edema occurring within 2 days (62–65). Neurologic signs and symptoms include headache, confusion, somnolence, or agitation (65–69). Severe neurologic conditions are commonly due to cerebral edema (66–69). Cardiopulmonary manifestations include pulmonary edema, decreased cardiac contractility, and pleural effusions (59,69,70). Decreased vascular resistance and increased leakage from the intravascular compartment lead to hypotension, which is one of the defining criteria for diagnosis (62,65,71). Hypotension with systolic blood pressure < 90 mm Hg or lower than the 5th percentile for children < 16 years can lead to tissue ischemia and organ failure (62,65,70).

Presence of a skin rash is another common finding in TSS. Initially, the rash will present as erythroderma, a diffuse, red, macular rash resembling sunburn, and can involve both the skin and mucous membranes (62,65). Mucous membrane involvement can include the conjunctiva, vaginal mucosa, or oral mucosa, producing a "strawberry tongue" (62,65,71). Superficial ulcerations occur in severe cases. However, the dermatologic findings can vary and may be subtle or