Toxic Shock Syndrome

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Continuing Education Activity

Toxic shock syndrome (TSS) is an acute-onset illness characterized by fever, hypotension, sunburn-like rash, and end-organ damage. TSS was classically associated with high absorbency tampon use in menstruating women until eventually, these were taken off the market. Since that time, it has become important to also consider non-menstrual cases. The incidence of TSS is estimated to be around 0.8 to 3.4 per 100,000 in the United States. This activity reviews the evaluation and treatment of toxic shock syndrome and discusses the role of the interprofessional team in evaluating and treating this condition.

Objectives:

- Summarize the etiology and pathophysiology of toxic shock syndrome.
- Review the history and exam findings of toxic shock syndrome.
- Describe the management of toxic shock syndrome.
- Explain the importance of improving care coordination among the interprofessional team to enhance the delivery of care for patients with toxic shock syndrome.

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Introduction

Toxic shock syndrome (TSS) is an acute-onset illness characterized by fever, hypotension, sunburn-like rash, and end-organ damage. TSS was classically associated with high absorbency tampon use in menstruating women until eventually, these were taken off the market. Since that time, it has become important also to consider non-menstrual cases. The incidence of TSS is estimated to be around 0.8 to 3.4 per 100,000 in the United States.[1][2][3]. Early recognition and antibiotic administration are key to improving patient outcomes and reducing mortality.

Etiology

TSS is most commonly caused by a toxigenic strain of *Staphylococcus aureus* or Group A Strep (*Streptococcus pyogenes*). Other strains of streptococci also produce superantigens, which can lead to TSS. The disease occurs most often in the setting of menstruation despite the discontinuation of high absorbency tampons. However, TSS can also present in non-menstrual settings such as in soft tissue infections, post-surgical infections, burns, retained foreign bodies such as nasal packing, and dialysis catheters. Staphylococcal TSS is typically the result of a localized infection such as an abscess, whereas streptococcal TSS may result from bacteremia, necrotizing fasciitis, or cellulitis.[4]

Epidemiology

The incidence of menstrual and non-menstrual TSS is estimated to be around 0.8 to 3.4 per 100,000 in the United States. The incidence tends to be higher in the winter and is more prevalent in developing countries. . Infants and the elderly are at highest risk for developing invasive Group A Strep infection, however between 1/5 and 1/3 occur in patients without any predisposing risk factors. [5]. The skin is the most common source/ risk factor for developing severe infection. [6]

Pathophysiology

TSS is a toxin-mediated disease that is caused by toxin-producing streptococci or *S. aureus*. These superantigens bypass the normal pathway for activation of T cells resulting in over-activation of cytokines and inflammatory cells. This then leads to the presenting signs and symptoms of fever, rash, hypotension, and end-organ failure due to capillary leak. Strep pyogenes (GAS) has other toxins that play a role in necrotizing fasciitis and streptococcal toxic shock syndrome. [5]

History and Physical

TSS typically presents with rapid onset of fever, rash, and hypotension. It may be preceded by a prodrome of fever and chills with nausea and vomiting as well as nonspecific symptoms such as myalgias, headache, or symptoms of pharyngitis (e.g., a sore throat, painful swallowing),

which then progresses to sepsis and organ dysfunction. Risk factors include superabsorbent tampon use, nasal packing, post-operative wound infections, recent influenza infection, as well as immunocompromised states.

The Center for Disease Control and Prevention (CDC) clinical criteria for TSS includes fever, rash, hypotension, and multisystem organ involvement. [5] Classically, the rash is a diffuse, blanching, macular erythroderma. Initially it may be a transient macular rash, predominantly on the chest. The rash desquamates one to two weeks later followed by full-thickness peeling. There may be mucosal involvement with strawberry tongue and ulceration of the vaginal mucosa or conjunctival erythema. Patients may exhibit disorientation or altered mental status without focal deficits. [7]

The CDC defines Streptococcal Toxic Shock Syndrome as an illness with the following[5][7]:

1. Hypotension defined by a systolic blood pressure less than or equal to 90 mm Hg for adults or less than the fifth percentile by age for children aged less than 16 years.
2. Multi-Organ Failure characterized by two of the following:
    - Renal impairment: Creatinine greater than or equal to 2 mg/dL (greater than or equal to 177 µmol/L) for adults or greater than or equal to twice the upper limit of normal for age. In patients with preexisting renal disease, a greater than twofold elevation over the baseline level.
    - Coagulopathy: Platelets less than or equal to 100,000/mm (less than or equal to 100 x 10/L) or disseminated intravascular coagulation, defined by prolonged clotting times, low fibrinogen level, and the presence of fibrin degradation products.
    - Liver involvement: Alanine aminotransferase, aspartate aminotransferase, or total bilirubin levels greater than or equal to twice the upper limit of normal for the patient's age. In patients with preexisting liver disease, a greater than twofold increase over the baseline level.
    - Acute respiratory distress syndrome: defined by acute onset of diffuse pulmonary infiltrates and hypoxemia in the absence of cardiac failure or by evidence of diffuse capillary leak manifested by acute onset of generalized edema, or pleural or peritoneal effusions with hypoalbuminemia.
    - A generalized erythematous macular rash that may desquamate.
    - Soft-tissue necrosis, including necrotizing fasciitis or myositis, or gangrene.

Laboratory Criteria for Streptococcal Toxic Shock Syndrome:

Isolation of group A Streptococcus

They then define the case as Probable if the case meets the criteria in the absence of another etiology and GAS isolated from a non-sterile site.

The case is defined as confirmed if GAS is isolated from a sterile site (blood, CSF, joint fluid, pleural fluid, or pericardial fluid) [5][7]

Evaluation

There is no specific lab test to identify TSS. A complete blood count (CBC) may show leukocytosis or leukopenia. Bandemia is common. Evaluation of multisystem organ involvement including CBC, CMP, CK, and coagulation studies should be drawn to evaluate for the clinical criteria of TSS. The CDC defines multisystem organ involvement as vomiting or diarrhea, myalgias, creatine phosphokinase (CPK) greater than two times the upper limit of normal, mucous membrane hyperemia (vaginal, oral, or conjunctival), BUN or creatinine two times the upper limit of normal, bilirubin or AST/ALT two times the upper limit of normal, Platelets less than 100,000, or altered level of consciousness without focal neurologic signs.[3][5][3]

Life-threatening hypocalcemia is prominent throughout the disease and should be repleted accordingly. Anemia, thrombocytopenia, and prolonged coagulation times are also common. Blood cultures and cultures from any suspected source should be obtained. Lumbar puncture should be performed in patients with fever and mental status change to evaluate for meningitis after obtaining coagulation studies.

Treatment / Management

Patients should receive aggressive intravenous (IV) fluid hydration with crystalloids. Soft tissue infections, especially necrotizing fasciitis should be sought out and managed. Any source of bacteria such as tampons or nasal packing should immediately be removed. Emergent surgical consultation should be obtained for any wound debridement or surgical cause. This is critical in the early management of toxic shock syndrome. [8][9]

Broad-spectrum antibiotics should be administered for those with an unidentified organism, if possible after blood cultures and cultures from the suspected source have been drawn. For most institutions, this will include vancomycin or linezolid given the high prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA). Clindamycin should also be administered to suppress toxin production. Studies have shown improved outcomes when Clindamycin is added to antibiotic regimens. [5][7][5] It should not be given alone as it is bacteriostatic, rather than bactericidal. Given that it is initially impossible to tell if the infection is polymicrobial, initial therapy should also cover gram-negative organisms.

Once the organism is identified, and sensitivities have been determined, antibiotics should be optimized and narrowed in the spectrum. Penicillin is the preferred antibiotic for group A strep. For MSSA, clindamycin is recommended, plus flucloxacillin or a beta-lactamase-resistant penicillin such as nafcillin. Current recommendations are to treat for seven to 14 days.

Vasopressors should be administered for patients with shock refractory to IV fluids. Most current guidelines recommend Norepinephrine as a first option. Intravenous immunoglobulin (IVIG) is thought to work by neutralizing the activity of the toxins produced and can be considered for shock refractory to fluids and vasopressors. While there are no randomized controlled trials supporting its use, observational trials have shown a reduction in mortality with IVIG compared to patients who only received antibiotics.[7] The optimal dosing is not well established, but high dose at 2 g/kg is acceptable. All patients should be admitted to an intensive care unit. Although a small study from 1984 showed reduced illness severity with steroids, there was no improvement in mortality. Corticosteroids are currently not recommended as adjunctive therapy for TSS.

Differential Diagnosis

- Scarlet fever
- Kawasaki disease
- Meningococcemia
- Toxic epidermal necrolysis
- Hemorrhagic shock
- Necrotizing Fasciitis/Gas gangrene
- Drug eruption
- Erythema multiforme

Prognosis

The case fatality rate of Streptococcal TSS may exceed 50%, particularly with delayed diagnosis; whereas non-streptococcal TSS is less than 3%. [7][5]

A small study in France showed that non-menstrual Toxic Shock Syndrome had a higher mortality (22%) than that of the menstrual toxic shock syndrome (0%). However, this was a small case series of 55 patients. [10]

Complications

Many of the complications from toxic shock syndrome are also part of the diagnostic criteria: end organ damage including renal failure, liver failure, coagulopathy, etc. In addition to these, glomerulonephritis and rheumatic fever can also occur.

Consultations

Almost all of these patients will require admission to the ICU, thus an intensivist should be consulted. Early surgical consultation should also be obtained, particularly given that the most common source is a soft tissue infection or wound, which may require debridement. Infectious Disease physicians can also assist with the appropriate antimicrobial regimen, particularly given the rarity of this disease.

Deterrence and Patient Education

Currently it is not recommended to provide prophylaxis for GAS to household contacts despite the increased risk of developing GAS. However, it is important to educate close contacts regarding the symptoms of GAS, and to recommend they seek care immediately should they develop. [11] [12] Those greater than age 65 are at higher risk of death from GAS, thus it may be reasonable to offer chemoprophylaxis to this population or those at higher risk for GAS.

At a minimum, standard precautions should be used in the hospital setting to prevent transmission to patients and staff. The CDC has

recommended for the first 24 hours of effective antibiotics to have the patient in both contact and droplet isolation. [5]

Pearls and Other Issues

All patients should be admitted to the intensive care until, with more severe cases going to a burn unit. The case fatality rate of Streptococcal TSS may exceed 50% whereas non-streptococcal TSS is less than 3%. The CDC does not recommend routine screening and chemoprophylaxis of household contacts of patients with invasive Group A Strep (GAS) infections.

In two large prospective trials, only five cases of invasive GAS occurred amongst almost 2000 household contacts. However, based on risk factors for death from invasive GAS, the CDC states “health care providers may choose to offer chemoprophylaxis to household members aged 65 years or those at increased risk of sporadic invasive GAS infection”. While there are no large trials with evidence-based regimens, should you choose to treat household contacts, seven to ten days of oral cephalexin is a reasonable choice. For additional information see the CDC case definitions for Toxic Shock syndrome (other than Streptococcal) and Streptococcal Toxic Shock syndrome.

Enhancing Healthcare Team Outcomes

Toxic shock syndrome is a life-threatening disorder which carries a very high mortality. While the mortality rates have decreased over the past 2 decades, they still vary from 1.8-12%. For those patients who are misdiagnosed or the treatment is delayed, the mortality can exceed 50%. For this reason, healthcare workers should be aware of the disorder and even if they do not manage it, should be able to make a prompt referral. The key in the management of TSS is prevention. The patient needs to be educated on the early signs and symptoms of the disorder and when to seek medical care. In some cases, chemoprophylaxis of household contacts of the patient is recommended. The moment TSS is suspected, even during triage to the emergency department, an infectious disease consultant must be called right away. Early surgical consultation in order to identify and manage source control is also critical to improving patient outcomes, as the most common source is a soft tissue infection or wound. These patients need rapid resuscitation and admission to the ICU. Only with aggressive treatment can the high mortality rates be prevented.[13] [14] (Level V)

Review Questions

- Access free multiple choice questions on this topic.
- Comment on this article.

Figure

Strawberry Tongue. Image of strawberry tongue caused by S*taphylococcus aureus* in a patient with toxic shock syndrome. Public Health Image Library, Public Domain, Centers for Disease Control and Prevention

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