**Staphylococcal Toxic Shock Syndrome**

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**Abstract**
A 28 year old male presented with fever, tachycardia, generalized lymphadenopathy and diffuse rash over the body. He failed to respond to intravenous antibiotics and developed cardiogenic shock, multiple organ failure and died within six hours after hospitalization. *Staphylococcus aureus* colonies were revealed on blood culture.

**INTRODUCTION**
Staphylococcal toxic shock syndrome (TSS) is a rare and potentially fatal multi system dysfunction. The syndrome occurs primarily due to TSS Toxin-1 (TSS-1) elaborated by *Staphylococcus aureus* (*S.aureus*). It occurs in diverse clinical settings, often mimicking common febrile conditions. The diagnosis depends chiefly on high degree of clinical suspicion. Thus doctors should be familiar with the manifestations of TSS and should vigilantly consider the diagnosis in appropriate clinical setting, as delay in diagnosis and/or in institution of appropriate therapy may result in fatal outcome.

**CASE REPORT**
A 28 year old male farmer presented to Emergency Room (ER) with moderate grade fever not associated with chills and rigors for five days and painful swelling of the left leg and right arm for three days. He also complained of diffuse rash, decreased urinary output, loose motions for two days and breathlessness for one day. On examination he was restless and had diffuse erythematous blanching rash predominantly involving the trunk and limbs. He had fever (103°F), warm pitting soft tissue edema over left leg and right arm and bilaterally enlarged submandibular, axillary and inguinal lymph nodes. Systemic examination revealed heart rate – 120/min, blood pressure (BP) - 110/40 mm Hg, respiratory rate - 40/min with decreased air entry in left axillary area. The patient was shifted to Intensive Coronary Care Unit (ICCU) and treatment was started with intravenous fluids, ceftriaxone and continuous dopamine infusion. Within couple of hours patient had altered sensorium, worsening of breathlessness, bilateral subconjunctival haemorrhage and hypotension (BP - 60/30 mm Hg). Subsequently fresh frozen plasma and platelet concentrates were infused, dopamine infusion rate was increased and patient was intubated. But he failed to respond to the line of management and went into cardiac arrest. Cardiopulmonary resuscitation was given, but the patient could not be revived and was declared dead.

Investigations revealed decreased white blood cell count [6000 cells/cmm (myelocytes-10%, stab-30%, neutrophils-36%, lymphocytes-4%, eosinophils-13%, monocytes-1%)] and decreased platelet count (80,000/cmm). Blood urea nitrogen (BUN) and SGOT (aspartate aminotransferase) were raised [47 mg/dl and 327 IU/L respectively]. Rest of the biochemical values were within normal limits. Urine examination revealed albumin-traces, granular casts-present, pus cells-5-6 per High Power Field (HPF), RBCs-1-2/HPF and epithelial cells-2-3/HPF. Both activated plasma thromboplastin time (APTT) and prothrombin time (PT) were raised, values being 1 min 15 secs and 22 secs respectively. Chest X-ray showed minimal left sided pleural infusion. *Staphylococcus aureus* colonies sensitive to oxacillin, cefazolin and vancomycin were obtained on blood culture. Smear for malarial parasite (SMP), IgM dengue, IgM leptospirosis and enzyme linked immuno sorbent assay (ELISA) for HIV were negative.

Post mortem report of inguinal lymph node and liver biopsy was inconclusive. Bone marrow examination revealed marked myeloid hypercellularity and increase in the number of coarse azurophilic granules in the cytoplasm of myeloid precursors (toxic granules). Staphylococcal toxic shock syndrome was considered as the cause of death.

**DISCUSSION**
Staphylococcal toxic shock syndrome (TSS) was first described by James Todd and colleagues in 1978 in children who presented with high fever, headache, confusion, conjunctival hyperemia, scarlatiniform rash, subcutaneous edema, vomiting, diarrhea, refractory
hypotension, oliguria and acute renal failure. Later on several reports described this disease in menstruating females using tampons in United States. Subsequently there has been many reports of non-menstrual TSS in adults as well as in children.¹

The disease does not show any racial, gender or age bias. The infection may occur in children, men, and non-menstruating women who have undergone surgery² or are immunocompromised in some way.

TSS is considered to be a superantigen-mediated disease where S. aureus toxins act as superantigens. These superantigens lead to a massive release of cytokines including tumor necrosis factor alpha (TNF-alpha), interleukin-1 (IL-1) and IL-6 which are responsible for a capillary leak syndrome leading to the development of the clinical signs of TSS.³ TSST-1 and staphylococcal enterotoxins are the major toxins associated with staphylococcal TSS.

Risk factors for the development of Staphylococcal TSS are tampon use, vaginal colonization with toxin-producing S. aureus and lack of serum antibody to the staphylococcal toxin. Staphylococcal TSS also has occurred following use of nasal tampons for procedures of the ears, nose and throat. Infection begins at a site of minor local trauma, which may be nonpenetrating. Cellulitis, subcutaneous abscesses, infected burns and pneumonia are some of the non-surgical focal infections associated with TSS. Viral infections such as varicella and influenza are sometimes responsible.

Clinical features⁴ include malaise, myalgias, diarrhea and chills which often precede the onset of the other physical manifestations of staphylococcal TSS. Fever, confusion and lethargy develop soon after the prodromal syndrome and is also associated with symptoms of hypovolemic shock related to capillary leakage and diarrhea. Hyperventilation, hypotension, tachycardia and erythematous rash are often seen on physical examination. The rash is usually diffuse macular erythema. Other signs include strawberry tongue, conjunctival hyperemia and edema of palms and soles. Hematologic, hepatic, muscular, renal, gastrointestinal and central nervous system involvement is common. Desquamation usually occurs one to two weeks after the onset of illness.

Currently, there is no diagnostic test for TSS. Identification of TSST-1 producing strains of S. aureus has been made possible by rapid and easily available Reversed Passive Latex Agglutination kit (RPLA) and other techniques like ELISA and radioimmunoassay; however these tests do not confirm toxin production in vivo. Recent studies show that the analysis of the Vbeta repertoire in patients with staphylococcal TSS is a potential diagnostic test.⁵ Staphylococcal superantigens activate specific fractions of the T-cell population by linking the Vbeta domain of the T-cell receptor. Each superantigenic toxin is associated with a characteristic Vbeta “signature”, analysis of which in vivo during TSS may facilitate the diagnosis. The test might be impractical in the Indian scenario, henceforth the diagnosis of TSS should be made exclusively on clinical grounds and isolation of S. aureus should be tried from body fluids wherever indicated.

Case definition of Staphylococcal TSS developed by the Centers for Disease Control and Prevention ⁶ includes major criteria, where all 4 conditions must be met i.e. fever: temperature >38.9°C (102°F), rash: diffuse macular erythema, desquamation: 1 to 2 weeks after onset of illness, particularly of palms and soles and lastly hypotension: systolic BP <90 mm Hg for adults or <5th percentile by age for children <16 yr of age or orthostatic syncope and minor criteria, where 3 or more of the following multisystems must be involved i.e. gastrointestinal: vomiting or diarrhea at onset of illness, muscular: severe myalgia or creatine kinase level twice upper limit of normal for laboratory, mucous membrane: vaginal, oropharyngeal, or conjunctival hyperemia. renal: BUN or creatinine level at least twice upper limit of normal for laboratory, or >5 white blood cells per HPF in absence of urinary tract infection. hepatic: total bilirubin, aspartate aminotransferase, or alanine aminotransferase at least twice upper limit of normal for laboratory, hematologic: platelets <100,000/mm³ and central nervous system: disorientation or alterations in consciousness without focal neurologic signs when fever and hypotension are absent.

Differential diagnosis

1. Streptococcal TSS: It is virtually identical, with the major difference being that the portal of entry, which cannot be proven in at least half the cases.
2. Leptospirosis (Weil’s disease): Generally causes icterus, headache and severe debilitating myalgias which were not seen.
3. Dengue shock syndrome: It could present with shock like state with the development of typical rash but on investigating IgM dengue antibody was negative.
4. Gram negative septicaemia: Blood culture did not show any gram negative organism.
5. Pneumococcal pneumonia: Chest X-ray picture was free of any pulmonary infiltrates making the diagnosis of pneumococcal sepsis unlikely.

Treatment

Treatment consists of immediate and aggressive management of hypovolemic shock. To ensure adequate perfusion of vital organs, fluid replacement with large volumes of crystalloid solutions or colloidal solutions is important and is considered the mainstay of treatment. Use of high dose penicillinase resistant penicillins like oxacillin or flucloxacillin, or β-lactamase inhibitor combinations like amoxicillin-clavulanic acid or ampicillin-sulbactam are recommended. Cefazolin
can be used in patients who are allergic to penicillin. Vancomycin or teicoplanin are drugs of choice in case of MRSA. Although corticosteroids were not considered an effective treatment, recently published case report 7 has highlighted the benefits of methylprednisolone in STSS, thereby opening a new window of hope in its management.

**REFERENCES**


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