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Case Report

A fatal case of staphylococcal toxic shock syndrome

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Case report

A 30 years old male patient fell down from a height of 5 ft and sustained injury on both the thighs and left knee. Four days later, he reported to a zonal hospital with complaints of tenderness both thighs and swelling of left knee. He was admitted as a case of 'Contusion knee with pyomyositis' and was managed conservatively with rest, nonsteroidal anti-inflammatory drugs (NSAIDs) and antimicrobials. After 24 h of admission, he developed fever, tachycardia, tachypnea, slurring of speech, confusion and features suggestive of acute renal failure and pulmonary thromboembolism. The same day he was transferred to this tertiary care center for further management. Examination revealed: temperature: 102 °F; pulse: 130/min; respiratory rate: 50/min and blood pressure: 84/50 mm Hg. Both the thighs were swollen and indurated (left more than right). Blanching erythematous rash was present all over the body. Therapy was instituted with combination of broad spectrum antimicrobials and dopamine in addition to other supportive measures. Within the next 6 h the condition of the patient deteriorated and was placed on ventilation. He became comatose and lapsed into hypotensive shock. Three hours later he suffered a cardiac arrest and expired. Detailed investigations were carried out in both the hospitals (Table 1). Clinical cause of death was recorded as: septic shock with multiorgan failure.

Introduction

Staphylococcal toxic shock syndrome (STSS) is an uncommon but potentially fatal disease with multisystem involvement. It occurs due to production of TSS Toxin-1 (TSST-1) by *Staphylococcus aureus* that induces a severe immunologically mediated inflammatory response affecting multiple organ systems and thereby mimics various diseases causing similar clinical picture. A high degree of clinical suspicion and prompt management is necessary to avoid fatality.¹ Herein we report a case encountered in our hospital.

Postmortem findings

An autopsy was conducted to ascertain the cause of death. Salient autopsy findings were as follows: well maintained

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Table 1 – Details of antemortem investigations.

Test	Findings
Hemoglobin (gm/dL)	13.5
TLC (per cmm)	5800
DLC (in %) and PBS	P-68, Band Forms-08, metamyelocytes-06, L-15, M-01, E-04; toxic granules ++
Platelets (per cmm)	135,000
Serum Bilirubin (mg/dL)	0.9
ALT (U/L)	264
AST (U/L)	178
Urea (mg/dL)	118
Creatinine (mg/dL)	2.0
Total CPK (U/L)	4054
CKMB (U/L)	160
X-ray chest	NAD
USG thigh	Cellulitis-bilaterally
Blood culture	<i>Staphylococcus aureus</i>

body with extensive diffuse blanching erythroderma over the shoulders, chest and arms; swelling of the left knee and both the thighs; papulovesicular lesions filled with clear fluid over posteromedial aspect of both the thighs; muscle tissue from both thighs were edematous and dusky in color. Deep incision into the muscle failed to reveal any pus pockets. Lt kidney showed dusky discoloration and necrotic areas on cut surface; lungs showed edema and consolidation. Great vessels were opened but no thrombi could be found. There was no bacterial growth from the aspirated fluid obtained from thigh; pericardial, peritoneal, pleural fluid. Aspirates from thigh muscle tissue and papulovesicular fluid too were sterile. Blood culture from heart and great vessels grew *S. aureus*. Histopathological findings included extensive parenchymal tissue destruction, vascular congestion and inflammatory cell collections composed primarily of lymphomononuclear cells including histiocytes in multiple organs namely lungs, kidneys, liver, spleen, pancreas, stomach and the intestines. Few scattered polymorphonuclear cell infiltration were also seen. Sections from thigh muscles showed myonecrosis, vascular congestion, focal hemorrhages and micro abscesses (Fig. 1).

Based on the clinical parameters, laboratory and postmortem findings this case was finally diagnosed as: death due to staphylococcal toxic shock syndrome (STSS).

Discussion

Toxic shock syndrome is the result of the immune system's reaction to one or more of a large family of true exotoxins referred to collectively as pyrogenic toxin superantigens (SAGs), which are produced by certain streptococci and staphylococci. The SAG exotoxin TSS toxin-1 (TSST-1) had been implicated in most cases of menstrual TSS (mTSS) and was designated SAG TSST-1.^{2,3} Nonmenstrual TSS is most often associated with *S. aureus* strains that make TSST-1, staphylococcal enterotoxin B (SEB), or staphylococcal enterotoxin C (SEC). Nonmenstrual TSS commonly follows bacterial super infection of the upper respiratory tract after viral infection. TSST-1 accounts for nearly 50% of all nonmenstrual TSS.

Considering the multiorgan involvement and the ability to mimic other diseases, the Centers for Disease Control and Prevention (CDC) published a case definition for streptococcal toxic shock syndrome in 1995 and updated it in 1996. In 1997, the CDC published a confirmed case definition for toxic shock syndrome (TSS) (Table 2).⁴

These superantigens evade the routine processing by antigen-presenting cells and interact directly with the invariant region of the class II major histocompatibility complex (MHC) molecule of the human T cells resulting in massive release of cytokines (cytokine storm).

Staphylococci are ubiquitous in nature, and about 75% of adults have antibodies against TSST-1, that increases to more than 90% by mid life.⁵ However, some persons fail to mount suitable antibody response to TSST-1 and are therefore more vulnerable to develop TSS and even recurrences due to lack of adequate antibody levels in their convalescent serum.⁶

Though menstrual-associated TSS affects only women, nonmenstrual TSS affects either gender equally. Staphylococcal TSS occurs primarily in patients aged 15–35 years. Since the young adults have the most vigorous immune system they are more likely to develop the full toxic shock syndrome. Furthermore, absence of antibodies to TSST-1 in young adults makes them vulnerable to STSS and recurrences too. Death is common in untreated cases.

In 1980, the rate of staphylococcal TSS in USA ranged from 2.4 to 16 cases per 100,000 of population.⁷ Subsequently, rates of menstrual-related TSS declined because of a decrease in the use of superabsorbent tampons. However with the emergence of 3 new MRSA strains namely USA 1100, USA 400 and USA 300 those have 10–100 times TSST-1 production capacity in vitro has led to an increase in prevalence of TSS from 0.8 per 100,000 in January 2000 to 3.4 per 100,000 in December 2003.^{8,9} However, the exact worldwide data on the prevalence of STSS is uncertain.

Ours is a confirmed case of STSS and in conformity with toxic shock syndrome (TSS), 1997 case definition, Centers for Disease Control and Prevention (CDC). This young man presented with the clinical signs of fever, hypotension, and diffuse macular erythroderma. Clinical and laboratory evidences of multiorgan involvement namely muscular, hepatic, renal and central nervous system were also present. Creatine phosphokinase was grossly raised. During the postmortem papulovesicular rashes in the inner thighs were demonstrated indicating early desquamation. Despite strong suspicion of cellulitis no pus collections were demonstrated and histopathology too did not demonstrate significant PMN infiltrations. However extensive tissue destruction in multiple organs and large collections of lymphomononuclear cells was present. Both these findings point toward a cytokine storm mediated reaction and concurrent suppression of PMN activity. *S. aureus* was isolated in both ante and postmortem blood samples (Table 2).

We reviewed the international and the national literature on TSS and specifically on STSS. Countries namely The United States, Australia, Denmark, Canada, Sweden, Japan and Netherlands maintain registry on TSS and issue surveillance report on TSS as per the International Classification of Diseases, 9th Revision (ICD-9). However, Indian statistics are limited.

Fig. 1 – H&E sections of various organs. HPE shows widespread tissue destruction, vascular congestion and lymphomononuclear cell invasion including histiocytes in liver, lungs, muscle, spleen, stomach and kidney. Sections from thigh muscles showed myonecrosis, vascular congestion, focal hemorrhages and micro abscesses.

Table 2 – Toxic shock syndrome (TSS), 1997 Case Definition, Centers for Disease Control and Prevention (CDC) and its conformity with our case.**Clinical case definition:**

An illness with the following clinical manifestations

1. Fever: temperature greater than or equal to 102.0 °F (greater than or equal to 38.9 °C) – **Yes**
2. Rash: diffuse macular erythroderma – **Yes**
3. Desquamation: 1–2 weeks after onset of illness, particularly on the palms and soles – **No**
4. Hypotension: systolic blood pressure less than or equal to 90 mm Hg for adults or less than fifth percentile by age for children aged less than 16 years; orthostatic drop in diastolic blood pressure greater than or equal to 15 mm Hg from lying to sitting, orthostatic syncope, or orthostatic dizziness – **Yes**
5. Multisystem involvement (three or more of the following):
 - (a) Gastrointestinal: vomiting or diarrhea at onset of illness – **No**
 - (b) Muscular: severe myalgia or creatine phosphokinase level at least twice the upper limit of normal – **Yes**
 - (c) Mucous membrane: vaginal, oropharyngeal, or conjunctival hyperemia – **Not known**
 - (d) Renal: blood urea nitrogen or creatinine at least twice the upper limit of normal for laboratory or urinary sediment with pyuria (greater than or equal to 5 leukocytes per high-power field) in the absence of urinary tract infection – **Yes**
 - (e) Hepatic: total bilirubin, alanine aminotransferase enzyme, or aspartate aminotransferase enzyme levels at least twice the upper limit of normal for laboratory – **Yes**
 - (f) Hematologic: platelets less than 100,000/mm³ – **No**
 - (g) Central nervous system: disorientation or alterations in consciousness without focal neurologic signs when fever and hypotension – **Yes**

Laboratory criteria:

Negative results on the following tests, if obtained:

- (a) Blood, throat, or cerebrospinal fluid cultures (blood culture may be positive for *S. aureus*) – ***S. aureus* isolated ante and postmortem**
- (b) Rise in titer to Rocky Mountain spotted fever, leptospirosis, or measles – **Negative**

Case classification:

Probable: a case which meets the laboratory criteria and in which four of the five clinical findings described above are present

Confirmed: a case which meets the laboratory criteria and in which all five of the clinical findings described above are present, including desquamation, unless the patient dies before desquamation occurs – **Confirmed case of STSS**

Conflicts of interest

All authors have none to declare.

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