

Staphylococcal Toxic Shock Syndrome In A 3-Year-Old Male Child

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Abstract

Staphylococcal Toxic shock syndrome is a life threatening, toxin mediated, and multi system illness caused by TSST 1 producing strains of Staphylococcus aureus. Though not infrequent in the paediatric population, there is a paucity of case reports in this age group. We report a case of toxic shock syndrome in a 3-year-old boy with fever, rash and hypotension and a focus of Staphylococcal infection in the jugulo digastric lymph nodes.

CASE REPORT

A 3 year old boy presented with intermittent, moderate grade, fever without chills & rigors and erythematous rash all over the body for 3 days, non bilious, non projectile vomiting for 2 days, watery stools, swelling of the face near the angle of jaw on the right side associated with redness and pain, refusal of feeds and lethargy for a day prior to admission. His past history was unremarkable. Growth & development were appropriate for age & sex.

At admission, he was toxic, drowsy and febrile with clinical signs of moderate dehydration. His vital signs were HR – 136 beats/min, RR – 32 breaths/min, Systolic BP – 61 mm of Hg and diastolic BP – 50 mm of Hg (< 5th percentile for age & sex).

On general physical examination, he had a 4 x 4 cm, tender, indurated, swelling in the right submandibular region along with an erythematous, macular rash all over the body, conjunctival congestion and palmar erythema. Abdominal examination revealed a palpable liver of 3 cm below the right costal margin and a palpable, soft spleen of 1 cm below the left costal margin along the spinoumbilical line. His Glasgow Coma Scale was 7/15, but focal deficits, features of meningeal irritation or raised intracranial tension were absent. Respiratory System and Cardiovascular System were normal on examination.

INVESTIGATIONS @ ADMISSION

Figure 1

Hb	: 9.9 gm / dl
WBC	: 8,700 cells / cumm
Platelet Count	: 1.5 lakhs / cumm
ESR	: 30 mm/hr
CRP	: 12.71 mg/L
PT	: 36.7 (Control 12.4)
APTT	: 79.4 (control 23.3)
FDP	: 3200 ng / ml
Serum Sodium	: 128.8 mEq / l
Serum Potassium	: 4.01 mEq / l
Serum Chloride	: 100.2 mEq / l
Liver function tests:	
Total bilirubin	: 1.2 mg / dl
Direct bilirubin	: 0.7 mg / dl
Indirect bilirubin	: 0.5 mg / dl
AST	: 297.6 IU / L
ALT	: 123.3 IU / L
ALP	: 121.5 IU / L
Blood Urea	: 127.5 mg / dl
Creatinine	: 2.44 mg / dl
Ultrasound Abdomen	: B/L renal parenchymal disease ?ARF

Clinical Photograph of the desquamation of the palms & soles of the child during 2nd week of onset of illness

Figure 2



Figure 3



Figure 4



CLINICAL COURSE

A diagnosis of Fulminant Sepsis with Disseminated

intravascular coagulation, Multiorgan Dysfunction Syndrome and Acute Renal Failure was considered initially and he was fluid resuscitated with Normal saline boluses. Simultaneously therapy with IV antibiotics {Cefoperazone-sulbactam and Ofloxacin – dosages were adjusted according to the calculated GFR}, Dopamine infusion at renal doses & diuretics was initiated. DIC was corrected with fresh frozen plasma transfusion and Vitamin K while dyselectrolytemia was managed with Sodium & Calcium supplements. Within 24 hours of admission, his urine output improved to 2.8 ml / kg / hr {Calculated GFR: 46 ml / min / 1.73 sqm}. Though he was hemodynamically stable, fluctuating consciousness level necessitated a CT scan of brain & neck and CSF analysis.

INVESTIGATIONS - DAY 1

Figure 5

Hb	8.2 gr/dl
WBC	23,000/cumm
Platelets	51,000 / cumm
S. Creatinine	0.98 mg / dl
Sodium	132.1 mEq / L
Potassium	3.18 mEq / l
Dengue IgM	Negative (6.7)
Leptospira IgM	Negative

Necrotic lymph nodes in right upper jugular chain with inflammation of adjacent soft tissue and arachnoid cyst in right temporal fossa (incidental finding) were evident on the CT SCAN brain and neck. CSF analysis was normal.

As all the clinical features pointed towards a diagnosis of Toxic Shock Syndrome, antibiotics were upgraded to IV Teicoplanin (dosage adjusted according to the calculated GFR) and 20 grams of IVIG was administered in 4 divided doses on the second day of admission. He was also transfused with Packed cells and Platelet concentrate. Repeat investigations showed Hb: 10.9g/dl, WBC: 23,300/cumm, platelets: 75,000/cumm, Sodium: 135.7mEq/l, potassium: 3.01mEq/l.

Frusemide was stopped as his urine output gradually improved to 6.6ml/kg/hr on the second day and nasogastric tube feed was commenced with Simyl MCT Formula. An ENT consultation was sought and a diagnosis of Acute tonsillitis (R>L) with Right jugulodigastric lymphadenitis was made.

Over the next five days, he gradually improved with defervescence of fever, decrease in the size of the swelling, disappearance of the erythematous rash with desquamation, improving oral intake, improving platelet counts and WBC

counts, normalization of renal parameters and coagulation profile. IV antibiotics were planned for 14 days and he was discharged home after 8 days. He developed desquamation of the skin of palms and soles during the second week of convalescence. Pus aspirated from the necrotic Right Jugulodigastric lymph node showed Gram-positive cocci in clusters - Staphylococcus thus confirming the diagnosis of Toxic Shock Syndrome. Absence of coronary aneurysms on 2D ECHO ruled out Kawasaki Syndrome.

DISCUSSION

Staphylococcal Toxic shock syndrome ^{1,2} is a multi system disease that can simulate many other systemic illnesses. Todd et al³ first described toxic shock syndrome in 7 children with high grade fever, erythroderma and shock in 1978. Shrock et al ⁴ first reported TSS associated with menstruation in 1980. Later on since 1980 increasing number of cases were reported in young menstruating women and the syndrome was found to be associated with the use of tampons ⁵ and barrier contraceptives including intra uterine devices ⁶. Nevertheless, it has also been described in men and children. In India, two cases of toxic shock syndrome in children were reported by Dass Rashna et al ⁷ in 2004. It can ensue as a super infection of skin lesions of many types including burns, insect bites, varicella lesions etc. Many cases of Staphylococcal TSS have been reported as a complication of influenza ⁸, pneumonia, empyema and sinusitis. Postoperative disease ⁹ has also been reported. It has also been reported following cantharidin application for molluscum contagiosum lesions ¹⁰. The diagnostic criteria laid down by CDC in 1980, include major, minor and exclusionary criteria ¹¹.

The incidence of Staphylococcal Toxic shock syndrome in children under 15 years is less than 0.05 cases per 100,000 population as reported by the CDC in 1999 ^{12,13}. A considerable number of the children with Staphylococcal Toxic shock syndrome are less than 2 years of age probably owing to the lack of antibody protection ².

Toxic Shock Syndrome is caused by exotoxin producing strains of Staphylococcus aureus. The most common toxins are the Toxic Shock Syndrome Toxin 1 (TSST 1) and the Staphylococcal enterotoxin. The pre requisites for the syndrome include colonization or infection of the individual by Staphylococcus aureus and lack of protective antibodies against the toxins. More than 90 % of adults have antibodies to TSS toxins ². The toxin being a super antigen does not require processing within the antigen processing cells before

presentation to the T cells. After binding directly to the MHC complex class 2, it stimulates an intense activation and proliferation of T cells and macrophages and

production of IL 1, IL 6 and TNF. It activates an alarming 30% of the total T cells unlike conventional antigens which can activate only 0.01 to 0.1% of the T cells. Thereby it causes capillary leak syndrome & massive loss of fluid from intravascular space which account for the disproportionate circulatory failure of the syndrome. ¹⁴

The clinical features of toxic shock syndrome typically include high-grade fever, generalized erythematous rash and hypotension with an identifiable focus of infection and late desquamation of the skin of palms and soles during convalescence. The circulatory failure is disproportionate to the apparent severity of the illness. Diagnosis of the syndrome is based on the criteria for case definition laid down by the CDC ¹¹.

MAJOR CRITERIA

Figure 6

Major Criteria	In this child
Fever: temperature $\geq 38.9^{\circ}\text{C}$ (102°F)	Yes
Rash: diffuse macular erythroderma	Yes
Desquamation: 1 to 2 weeks after onset of illness, particularly of palms and soles	Yes
Hypotension: systolic blood pressure ≤ 90 mm Hg for adults or <5 th percentile by age for children <16 yr of age, or orthostatic syncope	Yes

MINOR CRITERIA

Multisystem involvement (3 or more criteria must be met)

1. Gastrointestinal: vomiting or diarrhea at onset of illness
2. Muscular: severe myalgia or creatine kinase level twice upper limit of normal for laboratory
3. Mucous membrane: vaginal, oropharyngeal, or conjunctival hyperemia
4. Renal: blood urea nitrogen or creatinine level at least twice upper limit of normal for laboratory, or >5 white blood cells per high-power field in absence of urinary tract infection
5. Hepatic: total bilirubin, aspartate aminotransferase, or alanine aminotransferase at least twice upper limit of normal for laboratory

6. Hematologic: platelets <100,000/mm³
7. Central nervous system: disorientation or alterations in consciousness without focal neurologic signs when fever and hypotension are absent.

EXCLUSIONARY CRITERIA

Normal results on the following tests (if performed):

- Blood, throat, or cerebrospinal fluid cultures (blood culture may be positive for *S aureus*)
- Absence of other explanation for the clinical presentation.

TSS is potentially fatal. The minimum case fatality rate documented for Staphylococcal Toxic shock syndrome associated with menstruation is 2.5%, whereas for nonmenstrual cases it is as high as 6.4%.² The apparent causes of mortality are renal failure, myocardial dysfunction, coagulopathy, fluid overload, dyselectrolytemia (hypocalcaemia and hypomagnesaemia), encephalopathy and adult respiratory distress syndrome. Late complications include peripheral gangrene, reversible nail and hair loss, asthenia, muscle weakness and neuro psychiatric dysfunction¹⁴.

DIFFERENTIAL DIAGNOSIS

- Kawasaki syndrome: Kawasaki syndrome is the closest differential diagnosis of Toxic shock syndrome. But it is neither as severe nor as rapidly progressive. It is seen in children younger than 5 yrs. The differentiating features are absence of vomiting, diarrhea, myalgia, azotemia, hypotension, ARDS and shock in kawasaki syndrome. Thrombocytosis is a hematological marker of Kawasaki disease. TSS does not cause coronary aneurysms.
- Streptococcal Toxic shock syndrome: Associated with Streptococcal bacteremia or a focal streptococcal infection like cellulitis or pneumonia.
- Scarlet fever & Rocky Mountain Spotted Fever: Diseases not seen in India.
- Leptospirosis: The serology was negative for leptospirosis in this child.

- Toxic epidermal necrolysis: Clinical features were not suggestive of the same in this child.
- Measles: Clinical manifestations of the disease were not suggestive of measles in this child.

Diagnosed early and treated appropriately, complete recovery without sequelae is almost certain. Aggressive fluid resuscitation remains the cornerstone of treatment. Management regimen includes parenteral beta lactamase resistant anti staphylococcal antibiotics (Oxacillin, Nafcillin, Teicoplanin, Vancomycin, Clindamycin) for a minimum of 2 weeks, drainage of focally infected sites, appropriate management of hypotension, renal failure, cardiovascular collapse, Inotropic support and Intravenous Immunoglobulins. Dyselectrolytemia must be corrected. Children with TSS have poor humoral antibody response to TSST 1 in comparison to those without TSS. IVIG is known to boost up the antibody response. The indications for IVIG include requirement of inotropic support, mechanical ventilation, worsening renal function and in children with an undrainable focus of infection². The role of Corticosteroids is controversial.

This child presented to us with high-grade fever, generalized rash, loose stools, emesis and altered sensorium. On examination he was hypotensive and in peripheral circulatory failure. Investigations revealed elevated hepatic transaminases, abnormal renal functions and altered coagulation profile including thrombocytopenia. There was a focus of infection in the necrotic lymph nodes of jugulodigastric group on the right side and the tonsils. Gram stain of the pus aspirated from the lymph nodes showed Gram Positive cocci in clusters suggestive of Staphylococci. Blood cultures were sterile. He developed desquamation of the skin of palms and soles during the 2nd week of illness. 2D Echocardiogram done on follow up failed to show any coronary aneurysms. Thus this child met with all the major, 6 out of 7 of the minor and both the exclusionary criteria pertaining to the case definition of the syndrome. He responded well to aggressive fluid resuscitation, anti staphylococcal antibiotics and drainage of the suppurative lymph nodes. The child is on regular follow up now and is doing well.

CONCLUSION

Often not considered in the differential diagnosis, hence understandably under diagnosed and under reported, Toxic shock syndrome is a well described conglomeration of

clinical features and laboratory abnormalities. Anticipation of the possible complications and aggressive management with fluids, blood components, appropriate antibiotics, IVIG and immediate drainage of infected sites can lower the mortality and morbidity rates appreciably. A high index of suspicion and vigilance are required for early diagnosis as the disease has a close semblance to many other common febrile illnesses.

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