Toxic shock syndrome: an underdiagnosed illness – a case report

Cristiana Sousa, Carla Teixeira, Vasco Dias, Fernanda Almeida, Fátima Farinha

Abstract

Staphylococcal toxic shock syndrome is a rare and potentially fatal illness. Frequently the diagnosis is missed as the initial clinical features are non-specific. The progression to a toxic condition, caused by the systemic inflammatory response to toxins produced by bacteria, is rapid and unless definitive treatment measures are initiated in the early hours, the end result can be catastrophic due to multiple organ failure. We report a previously healthy patient who had features of toxic shock syndrome due to infection by *Staphylococcus aureus,* with multiple organ involvement, being treated successfully with antibiotics and aggressive care support. This case shows the high morbidity associated to this syndrome; however successful outcome is possible provided the patient is kept under close monitoring and proper early treatment is started.

Key words: Toxic shock syndrome, Systemic inflammatory response, multiple organ failure.

INTRODUCTION

TSS is a rare and potentially fatal illness (with a mortality rate as high as thirty percent), described for the first time in 1978,[1,2] in association with *Staphylococcus aureus* (*S. aureus*) infections.[2] During the 1980s, the number of diagnosed cases increased significantly, especially in young menstruating women, and an association with the use of super-absorbent tampons was suggested.[1,3,4]

Epidemiological studies, conducted subsequently, have linked TSS to other situations,[5,6] such as post-operative infections,[4,7] respiratory tract (sinusitis, tracheitis), skin, and soft tissue infections, intravenous drug use, and burns.[3] It has also been associated with infections caused by other agents, like *Streptococcus pyogenes* and *Clostridium spp*.[8]

While TSS may occur in individuals of any age, it is usually observed in healthy children and young adults[3].

Internal Medicine Service – Porto Hospital Center - Santo António Hospital

Received for publication on 28th April 2010
Accepted for publication on 15th July 2011

Clinical manifestations are due to the mass production of cytokines, also known as superantigens, by the T lymphocytes in response to the powerful toxins, also known as superantigens, released by the infectious agents.[1,9] S.aureus is capable of producing five enterotoxins (SE-A to E) and TSS toxin-1 (TSST-1). Most cases of staphylococcal TSS are mediated by TSST-1 and SEB and SEC, which lead to the release of TNF-α and IL-1, giving rise to fever, rash, hypotension, and tissue damage.[9]

It is characterized by acute onset, high fever, diarrhea, sore throat, hypotension, headaches, myalgia, and neurological symptoms.[1,9,10] Physical examination revealed signs of dehydration and generalized erythematous rash.

The symptoms often evolve to shock (ninety-five percent of cases), with hypoperfusion of the major organs, like the CNS and the kidneys. Respiratory failure and disseminated intravascular coagulation also occur in fifty-five percent of cases, and warrant admission to the Intensive Care Unit. The severity of multi-organ involvement is correlated with the degree of hypotension, and helps identify patients requiring hospitalization and more aggressive treatment.[9,10]

Peeling of the skin of the palms of the hands and soles of the feet is characteristic after two weeks.[1,9]

Laboratory results reflect an inflammatory response, in addition to the hypofusion of organs.[1,9]

Blood cultures are usually negative. The causative agent may be isolated in biological product collected at the initial site of infection.[9]

Since 1980, various definitions have emerged, the most consensual and most commonly used being

TABLE I

Diagnostic criteria for staphylococcal TSS*

Major **criteria**	***Minor*** **criteria**
Fever (≥ 38.5ºC) Hypotension: SBP ≤ 90 mmHg or orthostatic hypotension Diffuse macular rash Peeling of the skin of the palms of the hands and soles of the feet (convalescence)	Involvement of three or more of the following organs: Liver: bilirubin or AST/ALT** levels ≥ 2 x above normal Blood: platelets <100,000/ µl Kidneys: urea or creatinine ≥ 2x above normal or decrease in urine output Mucous membranes: vaginal, oropharyngeal, or conjunctival hyperemia Gastro-intestinal tract: vomiting or diarrhea Muscles: severe myalgias or CPK*** ≥ 2x above the normal value Central Nervous System: disorientation or alteration of consciousness without any focal neurological signs
Serology or other tests were negative for measles, leptospirosis, and Rocky Mountain spotted fever, and blood and CSF cultures were negative for other organisms besides *S. aureus*.	

*Based on CDC criteria (1997 update).
**Aspartate aminotransferase/Alanine aminotransferase.
***Creatine phosphokinase.

TABLE II

Evolution of analytical results

Laboratory data	On admission	24h later
Hematocrit (%)	34,2	27,7
Hemoglobulin (g/dL)	11,6	9,5
Leukocytes (per mm3)	13.20 x 10^3	7.29 x 10^3
Neutrofils (%)	97.7	92
Platelets (per mm3)	136.000	85.000
Prothrombin time (sec)	34,4 (↑7,4s)	32,2 (↑5s)
International Normalized Ratio (INR)	1,7	2,3
Glucose (mg/dL)	109	100
Sodium (mmol/L)	136	134
Potassium (mmol/L)	3,34	3,54
Urea (mg/dL)	38	48
Creatinine (mg/dL)	1,3	1,1
Bilirubin (mg/dL) Total Direct	 3,5 1,3	 3,6 1,7
Alkaline phosphatase (U/L)	24	33
Aspartate aminotransferase (U/L)	23	29
Alanine aminotransferase (U/L)	23	23
C-reactive protein (mg/L)	269	245
Lactic acid (mmol/l)	1,95	3,17

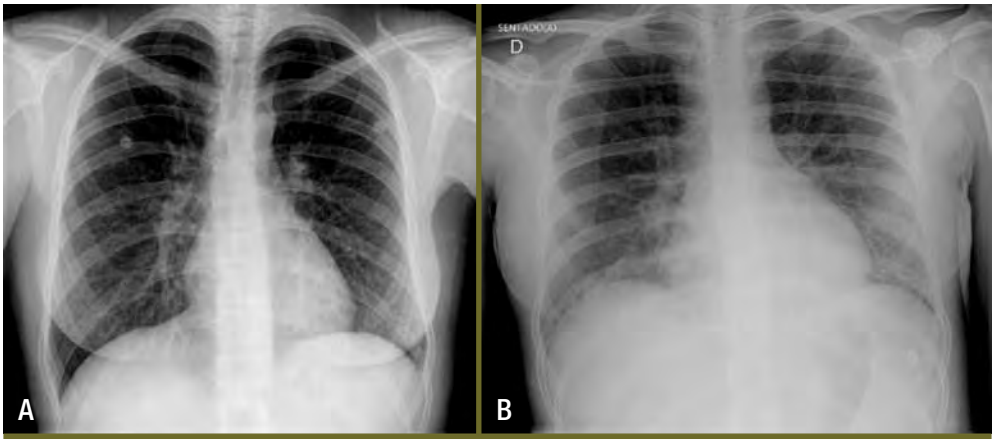
that given by the Center for Disease Control and Prevention (CDC).[9,10,11] Diagnosis is based solely on clinical and laboratory data and includes four major criteria (all of which must be present) and seven minor criteria, which reflect multisystemic involvement (at least three of which must be included).[1,9] The diagnostic criteria are summarized in *Table I*. Because TSS may mimic other common febrile profiles, ruling these out is essential. Thus, a differential diagnosis includes testing for meningococcemia, streptococcal infections (group A streptococcus), leptospirosis, Kawasaki syndrome, Rocky Mountain spotted fever, gram negative sepsis, exanthematous viral syndromes, and allergic reactions to drugs.[1,9]

In thirty to forty percent of cases, TSS may recur, and in women, the recurrence rate can reach as high as sixty percent during the six months following onset.[1,9]

CASE HISTORY

Woman, twenty-four years of age, previously healthy, taking an oral contraceptive (Yasmin®) regularly. Case of acute cystitis three weeks earlier, treated by the Attending Physician with co-trimoxazole, with resolution of the symptoms.

She went to the Emergency Service as a result of the acute onset of symptoms including fever, nausea, vomiting, diarrhea, bi-parietal headaches, neck pain, myalgia, sore throat, dry cough, and



Radiological evolution. A: Posteroanterior chest x-ray in the standing position – without pleuroparenchymatous lesions. B: Anteroposterior chest x-ray in decubitus, the twenty-four hours following admission – showing lower bilateral opacity.

FIG. 1

runny nose. She also reported two episodes, earlier that day, of faintness on standing. The symptoms began on the second day of her menstrual cycle, and the patient had a history of using absorbent tampons.

On admission, she was feverish (axillary temperature of 39.3ºC), tachycardic (115 bpm), hypotensive (80/50 mmHg), tachypneic (24 b/min), with 98% peripheral oxygen saturation at the room air. She also presented psychomotor retardation, disorientation, and full nuchal rigidity, but there were no focal neurological deficits. Ear, nose and throat tests showed ethmoid and maxillary rhinosinusitis with pharyngitis. No other alterations were noted in the physical exam.

Analytical changes present on admission are described in *Table II*. Urinalysis detected proteinuria (100 mg/dL) and erythrocyturia (10 to 25/field).

Cerebral computed tomography scan (CT) and cytochemical study of the cerebrospinal fluid were normal. Neither the abdomino-pelvic and renal ultrasounds nor the chest x-ray showed significant alterations.

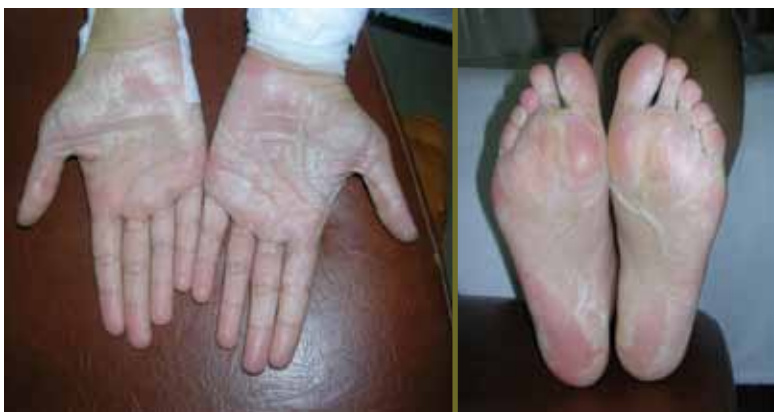
Given the clinical profile, early, aggressive volume replacement and empirical antibiotic therapy with amoxicillin and clavulanic acid (2.2g, administered parenterally, every eight hours) were started. However, the patient's condition quickly evolved to shock, requiring the support of pressoramines (dopamine, 5mcg/min) and she was admitted to the Intermediate Care Unit. During the next twenty--four to forty-eight hours, respiratory dysfunction, with type 1 respiratory failure and a pO2/fiO2 ratio of 243, and bilateral lower lung infiltrates (*Fig. 1*), consistent with acute lung injury and the worsening of the hematological dysfunction (*Table II*), were documented.

The antibiotic spectrum was broadened by adding meropenem (1 g, every eight hours, parenterally) and oxygen therapy was started.

Electrocardiogram showed normal sinus rhythm and there was no evidence of vegetations or ventricular dysfunction in the echocardiogram.

On the second day of hospitalization, the patient developed a macular rash on both her back and her extremities and a week later the peeling of skin from the palms of her hands and soles of her feet was observed (*Fig. 2*).

Methicillin-sensitive Staphylococcus aureus was isolated in the urine. The blood cultures were sterile, as were the microbiological CSF and sputum cultu-



Photographs of the hands and feet. Peeling of skin from palms of hands and soles of feet observed after one week of hospitalization.

FIG. 2

res. The stool study and Widal test were negative, as were the serologies for Leptospira and Rickettsia spp. Infection by the Human Immunodeficiency Virus was ruled out.

Evolution proceeded favorably, with gradual recovery of all the dysfunctions, and the patient was discharged after eighteen days in the hospital.

DISCUSSION

For the past thirty years, TSS has continued to be an important illness, yet because it is often underdiagnosed, its actual incidence is unknown.

Diagnosis is important, not only because of the associated morbidity and mortality, but also because of the high rate of recurrence. This patient developed a profile that rapidly evolved to multiple organ dysfunction (cardiovascular, respiratory, renal, hematological, neurological, metabolic, and digestive).

Early and aggressive intervention, as well as the proper monitoring of these patients, is critical.

The constellation of findings and the ruling out of other diagnoses made it possible to establish a diagnosis of staphylococcal TSS. ■

References

1. Todd J. Toxic shock syndrome. Clin Microbiol Rev 1988; 1: 432-446.

2. Todd J, Fishaut M, Kapral F, Welch T. Toxic shock syndrome associated with phage-group-I staphylococci. Lancet 1978; ii: 1116-1118.

3. Davis JP, Chesney PJ, Wand PJ, Laventure M. Toxic-shock syndrome: epidemiologic features, recurrence, risk factors, and prevention. N Engl J Med 1980; 303: 1429-1435.

4. Shands KN, Schmid GP, Dan BB et al. Toxic shock syndrome in menstruating women: association with tampon use and Staphylococcus aureus and clinical features in 52 cases. N Engl J Med 1980; 303: 1436-1442.

5. Reingold AL, Dan BB, Shands KN, Broome CV. Toxic-shock syndrome not associated with menstruation. A review of 54 cases. Lancet 1982; i: 1-4.

6. Reingold AL, Hargrett NT, Dan BB, Shands KN, Strickland BY, Broome CV. Nonmenstrual toxic shock syndrome: a review of 130 cases. Ann Intern Med 1982; 96: 871-874.

7. Morrison VA, Oldfield EC. Postoperative toxic shock syndrome. Arch Surg. 1983; 118: 791-794.

8. Fischer M, Bhatnagar J, Guarner J, Reagan S, Hacker JK. Fatal Toxic Shock Syndrome Associated with Clostridium sordellii after Medical Abortion. N Engl J Med; 2005. 353:2352-2360.

9. Habif TP. Exanthems and Drug Eruptions. In: Habif TP, ed. Clinical Dermatology. 5th ed. Philadelphia, Pa: Mosby Elsevier; 2009: chapter 14: 544-580.

10. Chesney PJ, Davis JP, Purdy WK, Wand PJ, Chesney R W. Clinical manifestations of toxic shock syndrome. J. Am. Med. Assoc. 1981. 246:741-748.

11. Wiesenthal A M, Ressman M, Caston S A, Todd J K. Toxic shock Syndrome. I. Clinical exclusion of other syndromes by strict and screening definitions. Am. J. Epidemiol. 1985. 122:847-856.