

A case of non-menstrual toxic shock syndrome

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Abstract

A 20-year-old woman was admitted with a short history of high fever, rash, gastrointestinal symptoms, vaginal discharge and hypotension. Whilst toxic shock syndrome was considered, no gynaecological source of infection was found. Subsequent isolation of *Staphylococcus aureus* from a cutaneous blister led to confirmation of the diagnosis.

Keywords

Toxic shock syndrome; *Staphylococcus aureus* toxinaemia.

Case history

A 20-year-old woman was admitted with a 2-day history of intermittent colicky lower abdominal pain, nausea and vomiting, watery diarrhoea, fever and rigors. She had not travelled abroad recently, and had no known infectious contacts. She had used tampons for her last menstrual cycle 3 weeks prior to admission. The only other history of note was that she had purchased a pair of new shoes 1 week prior to admission, and had developed small blisters on the inner aspect of both heels. She had no past medical history of note, was not on any regular medications and denied any recreational drug use. Of importance was the fact that she was given one intravenous dose of cefotaxime by paramedics who transferred her to the emergency department.

Baseline observations revealed a temperature of 40°C, blood pressure 87/34 mmHg and pulse 130 beats/min. She was clinically dehydrated. There was a mild, erythematous, macular rash over the legs, chest and face. She had small non-tense bilateral heel blisters around 1 cm in diameter. Cardiorespiratory, abdominal, neurological and joint examination was unremarkable, and Glasgow Coma Score was 15. Pelvic examination revealed some white vaginal discharge, but no tampon *in situ* and no adnexal tenderness or cervical excitability.

Blood results showed: haemoglobin 10.1 g/dl (11.5-16.5 g/dl), white cell count $17 \times 10^9/l$ ($4.0-11.0 \times 10^9/l$), neutrophils $16.3 \times 10^9/l$ ($2.0-7.5 \times 10^9/l$), platelets $209 \times 10^9/l$ ($150-400 \times 10^9/l$). Arterial pH, serum lactate, urea and electrolytes were all in the normal range. Urinalysis showed leucocytes, protein, ketones and mild microscopic haematuria. A chest radiograph showed no abnormalities.

In view of her evidence of severe sepsis, she was admitted to the high dependency unit and resuscitated with intravenous fluids. She was penicillin allergic, and following microbiological advice, she was commenced on intravenous amikacin, clindamycin, vancomycin and metronidazole for presumed toxic shock syndrome (TSS). Despite treatment her clinical state deteriorated, necessitating transfer to intensive care for inotropic support and ongoing fluid management, although she did not require ventilation or renal support. Multiple blood, urine, and stool cultures did not grow any bacteria, and viral serology was negative, although as antibiotics were administered by the paramedics on her transfer to hospital, lack of growth in bacterial culture not surprising. Contrast tomography of her chest, abdomen and pelvis was normal. She developed a thrombocytopenia and raised transaminases which were transient and probably due to the TSS. Over the next 10 days, her clinical state improved with intravenous antibiotics, although it was noted that the right heel blister was enlarging. Fluid taken from this blister was noted to be purulent, and cultures grew *Staphylococcus aureus*. The isolate was sent to the Staphylococcal Reference Laboratory (Health Protection Agency Centre for Infections, Colindale) for *S. aureus* toxin gene detection studies. This revealed that the organism was positive for TSS toxin-1 (tst gene) and Enterotoxin C (sec gene).

The blister was allowed to drain, and she was discharged 12 days after admission. Prior to discharge, she developed desquamation of skin from her palms and soles. At review, she remained clinically well and fully recovered.

Discussion

TSS was first described in children in the late 1970s, and subsequently an association with tampon use by menstruating women in the early 1980s. Most cases are related to the staphylococcal toxin, TSS toxin-1 (TSST-1). The other toxins include Enterotoxins B and C, which occur much more frequently in non-menstrual TSS and are important to its pathogenesis. The syndrome is characterised by a severe systemic inflammatory response caused by certain strains of toxin producing *S. aureus* and *Streptococcus pyogenes* (group A streptococcus). Toxins produced by these organisms act as superantigens, stimulating release of massive amounts of pro-inflammatory cytokines, leading to a severe inflammatory response, leading to severe shock and frequently multi-organ failure^[1]. The hallmark features of a patient presenting with *S. aureus* TSS are high fever, rash and hypotension. These will usually be preceded by a short history of general malaise, gastrointestinal disturbance and dehydration^[2].

The Centre for Disease Control and Prevention have described some diagnostic criteria for *S. aureus* TSS (Table 1)^[2]. They suggest that confirmation of TSS requires all the major criteria listed, plus any three or more of the minor criteria. Laboratory abnormalities that are found in more than 85% of the affected patients include hypoalbuminaemia, hypocalcaemia, elevated liver enzyme levels, thrombocytopenia, pyuria, proteinuria, and elevated creatinine levels^[3]. Blood cultures are positive in only 5–15% of patients with TSS^[1].

It is widely assumed that TSS is always gynaecological in origin and associated with tampon use in menstruating women. It is now clear the syndrome can affect many people, with no relation to

Table 1. Criteria for the diagnosis of toxic shock syndrome

Major criteria	Minor criteria (3 or more of following)
Fever >38.8°C	Gastrointestinal (vomiting or diarrhoea at illness onset)
Erythematous rash; skin desquamation 1-2 weeks after onset of illness	Central nervous system (disorientated or alterations in consciousness without focal neurological signs when fever and hypotension are absent)
Hypotension (systolic <90 mmHg)	Mucous membrane hyperaemia
	Muscular (severe myalgia or raised creatine kinase levels at least twice upper limit of normal)
	Hepatic (thrombocytopenia, liver function tests twice upper limit normal)
	Renal impairment (urea or creatinine twice upper limit of normal)

menstruation. Indeed, around half of all cases of TSS occur in non-menstruating women^[4]. Due to the systemic inflammatory response of the body to the toxins, TSS has a wide differential diagnosis as it can mimic other more common conditions, such as acute pyelonephritis. In patients presenting with a severe febrile illness out of keeping with local findings, TSS should always be considered in the differential diagnosis.

Cutaneous staphylococcal infection can rarely cause TSS, and it is imperative that a thorough clinical examination is carried out to identify potential foci of staphylococcal infection, as most non-menstrual TSS is due to a cutaneous source. Drainage of even small areas of infected tissue, such as abscesses or blisters is required as this may provide the portal of entry of the organism in to the systemic circulation and cause overwhelming inflammatory response^[2]. It has been suggested that in non menstrual TSS focal signs of infection are usually minimal or absent, and mortality is higher^[5]. Our patient presented with small localised blisters on the heels which were not thought to be clinically significant at presentation, but turned out to be the source of infection.

Teaching points

TSS is an uncommon clinical syndrome presenting with high fever, rash, hypotension and gastrointestinal symptoms. Presentation with an erythematous rash and skin desquamation 1-2 weeks after the onset of the infection is a hallmark of the condition. Whilst menstruating women are more commonly affected, a significant number of cases are not due to gynaecological infection. Early recognition of TSS is essential in order to treat the condition rapidly and prevent mortality or morbidity.

References

1. Sharma S, Harding G. Toxic shock syndrome. E-Medicine. October 2006. <http://www.emedicine.com/med/topic2292.htm> (accessed 25 July 2008).
2. Todd JK. Toxic shock syndrome. Clin Microbiol Rev 1988; 1: 432-46.
3. Chesney PJ, Davis JP, Purdy WK, Wand PJ, Chesney RW. Clinical manifestations of toxic shock syndrome. JAMA 1981; 246: 741-8.
4. Colbry SL. A review of toxic shock syndrome: the need for education still exists. Nurse Pract 1992; 17: 39-46.
5. Descloux E, Perpoint T, Ferry T *et al*. One in five mortality in non-menstrual toxic shock syndrome versus no mortality in menstrual cases in a balanced French series of 55 cases. Eur J Clin Microbiol Infect Dis 2008; 27: 37-43.