Toxic Shock Syndrome

Synonyms: TSS, streptococcal toxic shock-like syndrome (STSS), 'toxic strep'

Definition
Toxic shock syndrome (TSS) is a multisystem inflammatory response to the presence of bacterial exotoxins.

Todd first described it amongst children in 1978; the toxins were secreted by *Staphylococcus aureus*. Subsequently it was found to be associated with tampon use in menstruating women and Group A streptococcal infections - the streptococcal toxic shock-like syndrome (STSS). It is now recognised as a consequence of a range of infections associated with toxin-secreting staphylococci and streptococci. Enhanced surveillance of the rate of Group A infections is undertaken by microbiologists in the UK and several European countries.

Pathogenesis
The infecting staphylococcal or streptococcal exotoxin acts as a superantigen, setting off a reactive inflammatory cascade, mediated predominantly by tumour necrosis factor alpha and interleukin-1.

Epidemiology
In the early 1990s there were roughly 40 cases per year in the UK, with 2-3 deaths per year. This has since declined due to change in tampon manufacture, and increased awareness.

Group C and Group G streptococci have been reported to cause invasive disease similar to that classically associated with group A streptococcus.[1,2]

- The incidence of both TSS and STSS appeared to increase through the 1980s and 1990s but has now stabilised. A UK series showed an incidence of STSS increasing from 1 to 9.5 per million population per year in the 1990s.[3]
- Infections not associated with menstruation have become more common as menstrual cases have declined. The incidence in children is lower than that in adults.[4]
- Both conditions are relatively rare; worldwide background prevalence of TSS is approximately 3/100,000 people.[5]

Possible risk factors
- *S. aureus* cellulitis.
- Wounds (including burns).
- Tampon use (now less relevant) or gynaecological infection.
- Puerperal sepsis.
- Postoperative infections (classical signs of infection may be absent in wound).
- Packed wounds - eg, nasal.
- Sinusitis.
- Tracheitis.
- Recreational intravenous drug use.
- HIV.
- Allergic contact dermatitis.
- *Varicella* spp.
- Influenza A virus.
- There is debate around an association with non-steroidal anti-inflammatory drug use.[4]
Presentation

Presentation is usually nonspecific and patients generally present with flu-like symptoms and can develop a life-threatening TSS in just a few hours. Features may include:

- Fever: this is usually high at approximately 39ºC.
- Rash: this is usually diffuse, macular and erythodermic (intense widespread reddening of skin). A scarlatiniform eruption, ie widespread fine, red, papular - 'sandpaper-like' with flexural accentuation, may also be seen.
- Hypotension: this may be profound and is due to suppression of myocardial contractility by the toxin.\textsuperscript{[7]}
- Multiorgan dysfunction.
- Desquamation of palms and soles of feet 1-2 weeks after onset.
- Palms, soles of feet, mucous membranes and tongue may be bright red.
- Nausea, vomiting and diarrhoea are relatively frequent presenting features.
- Myalgia and muscle weakness are common.
- Confusion and disorientation may indicate encephalopathy.

Examination should seek evidence of the source of the infection by:

- Close examination of the skin.
- Checking for tampons; gynaecological examination.
- Respiratory examination.

Differential diagnosis

- Cellulitis.
- Any patient with a fever and a rash.\textsuperscript{[8]}
- Meningococcal disease.
- Gram-negative septic shock.
- Erythema multiforme/Stevens-Johnson syndrome/toxic epidermal necrolysis (as drug reaction).
- Heat-related illness.
- Infectious mononucleosis.
- Infective endocarditis.
- Kawasaki disease.
- Viral infection and exanthem.
- Leptospirosis.
- Typhus/other rickettsial infections.
- Cardiogenic shock.
- Listeria monocytogenes infection.
- Typhoid.
- Dengue fever.

Investigations

- Blood cultures are positive in 5-15% of cases of TSS and in approximately 50% of STSS.
- FBC often shows leukocytosis and low platelets.
- U&Es may show raised urea and creatinine, electrolyte disturbance and hypocalcaemia.
- CK and LFTs may be elevated.
- Urinalysis may show microscopic haematuria/myoglobinuria.
- Any wounds should be swabbed for culture.
- Throat swab/others as per clinical suspicion of focus of infection.
- CXR may be useful if there is suspected pneumonic focus.
Management

Early diagnosis and rapid intervention are the key to arresting the cascade of inflammation that leads to rapid deterioration:

- Any persistent focus of infection, such as abscess, wound pack, wound slough or tampon, should be removed immediately, with surgical assistance if necessary.
- Aggressive haemodynamic resuscitation, preferably with central fluid volume monitoring and regular electrolyte testing is crucial.
- Vasopressor agents may be used to manage shock, under expert guidance.
- Any abnormality of glucose levels should be closely managed and normalised.[9]
- Antibiotics should be given early and in sufficient doses:
  - Choice of agent depends on suspected pathogen and local patterns of prevalence and resistance.[10] Cephalosporins and clindamycin provide broad cover that should be effective against relevant organisms.[5]
- Steroids may play a role in improving survival.[11] Research has shown that a long course of low-dose corticosteroids reduces 28-day all-cause mortality, and intensive care unit and hospital mortality.[12]
- There is no evidence for the use of activated protein C for treating patients with severe sepsis or septic shock. Activated protein C was therefore withdrawn in 2011.[13]

Prognosis

- Mortality rate for TSS is around 5-15%.
- A fatality rate of up to 64% has been noted in cases of STSS in the UK.[3]
- Recurrence of TSS is found in 30-40% of cases.

Complications

- Recurrence.
- Cardiomyopathy.
- Rhabdomyolysis.
- Acute kidney injury.
- Encephalopathy and cerebral oedema.
- Acute respiratory distress syndrome.
- Hepatic necrosis.
- Thrombocytopenia and narrow suppression.
- Disseminated intravascular coagulopathy (DIC).
- Metabolic acidosis, electrolyte disturbance.

Further reading & references

- Toxic Shock Syndrome Information Service
  10. British National Formulary

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