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Case report

Non-menstrual associated toxic shock syndrome

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A 40-year-old female patient developed toxic shock syndrome following breast surgery. A toxin producing strain of *Staphylococcus aureus* was isolated from the post-operative wound.

INTRODUCTION

The term toxic shock syndrome (TSS) was first used in 1978[1] to describe a condition characterised by sudden onset of fever, shock, confusion, subcutaneous oedema, erythematous rash which desquamates in convalescence, abnormalities of many other systems, and negative blood culture. These effects are thought to be due to circulating staphylococcal toxins arising from a focus of staphylococcal infection. It has most commonly been associated with the use of certain types of tampons during menstruation, but is now increasingly being recognised in up to 13% of cases in a variety of clinical situations not associated with menstruation.[2] *Staphylococcus aureus* has been associated with TSS and most strains isolated from patients with this syndrome have produced enterotoxin F or pyrogenic exotoxin C, now thought to be the same toxin and renamed Toxic Shock Syndrome Toxin-1 (TSST-1). However, other strains of *Staphylococcus aureus* implicated in the syndrome have produced different toxins, particularly enterotoxins B and C[3] in non-menstrual cases. Mortality is higher in these cases with non-TSST-1 producing strains than with TSST-1 producing strains.[4] We report here a patient who fulfilled the case definition of the Center for Disease Control, Atlanta, USA,[5] and which we believe is the first case notified in Northern Ireland.[6]

CASE HISTORY

A 40-year-old woman was admitted to another hospital for removal of a breast lump. Surgery was uneventful and she was discharged the following day. The biopsy was subsequently reported as benign fibroadenosis. Two days later the patient was readmitted with pyrexia (40°C), hypotension (90/40 mmHg), and an erythematous rash on the trunk which spread rapidly to all limbs over the next two days. The patient was commenced on benzyl penicillin and gentamicin for a presumed diagnosis of septicaemia, possibly meningococcal.

Two days after this second admission the patient was transferred to the intensive care unit of this hospital. The breast wound, although not painful, exuded a slight

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discharge from which *Staphylococcus aureus* was cultured and the antibiotic therapy was changed to flucloxacillin and gentamicin on the advice of the bacteriologist.

Other clinical features included vomiting, periorbital oedema, pulmonary oedema, leg muscle myalgia, confusion, and disorientation in time and place. Laboratory investigations showed a leucocytosis ($20 \times 10^9/l$), impaired renal function (creatinine 395 μmol/l), and impaired hepatic function (bilirubin 64 μmol/l, aspartate transaminase 184 μmol/l, alanine transaminase 70 μmol/l, and lactate dehydrogenase 595 μmol/l). There was also an elevated creatinine kinase (1589 μmol/l), a decreased serum calcium (1.68 mmol/l), and an increased serum phosphate (1.6 mmol/l). The haemoglobin dropped from 12.5 g/dl to 9.2 g/dl over 48 hours without any signs of blood loss but this may have been contributed to by a dilutional effect. A coagulopathy was detected with a partial thromboplastin time of 72 seconds (control 44s), a fibrinogen degradation products level of 32 μg/ml (normal 0 – 8) and a low platelet count ($105 \times 10^9/l$). All these features are characteristic of TSS.

On the eighth post-operative day the rash had faded considerably and there had been no pyrexia for 48 hours. However, the creatinine continued to rise (418 μmol/l) and dopamine was still required to maintain the blood pressure at 100/70 mmHg. The patient was then taken back to theatre for exploration of the breast wound in which considerable necrosis was observed and *Staphylococcus aureus* was re-isolated from the wound.

The patient made a gradual recovery over the next few weeks. Desquamation occurred throughout the area of distribution of the rash starting two weeks after the rash had disappeared and continuing for three weeks into convalescence. This was followed by marked hair and nail loss with subsequent regrowth after several months. These are the convalescent features characteristic of TSS. The patient was discharged one month after admission.

BACTERIOLOGY

The strain of *Staphylococcus aureus* isolated from the wound was non-typable by phage typing at the routine test dose ×100. It was sensitive to benzyl penicillin with a minimum inhibitory concentration (MIC) of 0.125 μg/ml and a minimum bactericidal concentration (MBC) of 0.25 μg/ml, and also to flucloxacillin (MIC 0.5 μg/ml and MBC 0.5 μg/ml). Screening swabs from various carriage sites did not produce similar strains of *Staphyloccocus aureus.* A *viridans* group streptococcus was isolated from one of four blood culture bottles taken on the day of re-admission, but this was not considered clinically relevant. *Staphylococcus aureus* was not isolated from blood culture.

Toxin studies are not routinely available but tests carried out at a reference laboratory showed that this strain of *Staphylococcus aureus* did not produce TSST-1, but did produce enterotoxin C. Limited serum antitoxin studies in both acute and convalescent sera showed the presence of antibody to TSST-1 and to enterotoxin B but not against enterotoxin A. Unfortunately antibody studies against enterotoxin C and other toxins were not available in the reference laboratory.

DISCUSSION

Up to 15% of some reported series of non-menstrual TSS have followed surgery, from which a median incubation period of two days has been estimated.[2]

Typically, the wound is not painful nor clinically suspicious of being infected. Other cases have been described, associated with subcutaneous abscesses, cellulitis, infected insect bites, hydradenitis suppurativa, an infected cutaneous ulcer and an infected burn.[2]

Menstrual and non-menstrual associated TSS strains appear to have different bacteriological features. In this case, the strain of *Staphylococcus aureus* was not phage-typable. Epidemiological studies have shown that strains of *Staphylococcus aureus* in menstrual associated TSS are usually in phage group 1,[4] and non-menstrual associated TSS strains are either in other phage groups or are not phage-typable. Also, this strain did not produce TSST-1 and did produce enterotoxin C. Although TSST-1 is produced by about 90% of strains from reported cases of menstrual associated TSS, it is only associated with about 60% of non-menstrual associated cases, and it has recently been suggested that its role is not essential in the pathogenesis of TSS and that other as yet unrecognised toxins may play a part.[4]

Antibodies may have a protective role, as 88% of control group patients have antibody titres to TSST-1,[7] whereas only 18% of acute phase sera[8] and 20 – 30% of convalescent sera of all TSS patients show antibody to TSST-1.[9] Patients with TSS would appear to have a defect in the anti-TSST-1 immune response as shown by the low percentage of patients who seroconvert. The antibody titres in these patients are also much lower than those of control sera.[3] This may also explain the high recurrence rate of 28% in the same individual patients.[5] Significant antibody titres to TSST-1 are present in normal human immunoglobulin[10] and this may have a therapeutic role in the future when the causative toxin has been more clearly identified.

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