

# Streptococcal toxic shock–like syndrome in a post-myomectomy patient

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**We report on a healthy 34-year-old woman who received an elective myomectomy for uterine fibroid, and postoperatively developed fatal streptococcal toxic shock–like syndrome. We discuss the series of events that led to this life-threatening disease and its pathophysiology, and suggest areas in which management might have been improved.**

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*Key words: Fatal outcome; Postoperative complications; Shock, septic; Streptococcus pyogenes*

## Introduction

Streptococcal toxic shock–like syndrome is an acute, rapidly progressive, and often fatal illness. It is an uncommon form of septicaemia caused by *Streptococcus pyogenes* (Lancefield group A), which is also the pathogen responsible for scarlet fever and other streptococcal soft tissue infections. As with staphylococcal toxic shock syndrome, invasive streptococcal diseases are also caused by biologically potent exotoxins that mediate fever, shock, and tissue injury.

There has been a significant reduction in the incidence and severity of streptococcal infection throughout most of the 20th century.<sup>1</sup> The main reason for this decline is the introduction of penicillin in 1945 and the subsequent development of other antibiotics. In the late 1980s, however, *S. pyogenes* has re-emerged with renewed virulence and has posed a global public health problem.<sup>2</sup>

Sporadic outbreaks of a rapidly progressive disorder that is often associated with severe suppurative soft tissue infection, and is characterised by fever, desquamating rash, and multi-organ system failure, have recently been reported in young, otherwise healthy adults.<sup>3</sup> In this report, we describe a young, healthy woman who

developed streptococcal toxic shock–like syndrome (TSLS) after undergoing a routine myomectomy.

## Case report

A 34-year-old Chinese woman presented to Kandang Kerbau Hospital in March 1995 with lower abdominal discomfort that had lasted 1 week. She also gave a history of primary subfertility for 9 years and allergy to tetracyclines. Physical examination revealed an otherwise healthy, 49-kg woman. Pelvic examination and ultrasonography showed a uterine fibroid of 14 weeks' size. The patient was then scheduled for an elective myomectomy. A urine pregnancy test was negative.

Preoperatively, the patient was assessed as fit; she did not give any history of recent upper respiratory tract infection. The 1-hour myomectomy was performed under general anaesthesia; there was minimal blood loss during the operation. The uterine cavity was not entered and a 15-cm pedunculated subserosa fibroid was removed. Postoperatively, she was sent to the general ward for observation, and a 24-hour continuous intravenous morphine infusion was prescribed for pain relief. Additional analgesia (pethidine 50 mg) was given on the first and second postoperative days by intramuscular injection into the right thigh.

The patient recuperated well except for three febrile episodes on the first, second, and fourth postoperative days. Each episode was relieved quickly by giving mefenamic acid, acetaminophen or cold compress. By then, she was eating well and was

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ambulatory. In the evening of the fourth postoperative day, she complained to her family of pain over the right thigh, near the former sites of intramuscular injection. On the morning of the fifth postoperative day, the patient's general condition worsened. She had a temperature of 39.5°C, had vomited, and complained of abdominal discomfort and pain over the anterior aspect of the right thigh. Examination revealed normal vital signs and a slightly inflamed patch over the anterior aspect of the right thigh. Intravenous ampicillin 500 mg and cloxacillin 500 mg were given in the view of a possibility of cellulitis in the thigh. The two previous injection sites (over the lateral aspect) were inspected and found to be clean.

Three hours later, the patient's condition suddenly deteriorated. She became very distressed and hypotensive. Examination revealed a blood pressure of 90/50 mm Hg and a pulse rate of 110 beats per minute. The abdomen was distended and tender, but there were no bowel sounds. The right thigh was swollen and there was a bluish hue that spread distally over the groin. The clinical impression was that of hypotensive shock, probably secondary to intra-abdominal haemorrhage, with blood tracking down the right leg. An emergency laparotomy was scheduled immediately. On arrival in the operating theatre, the patient was awake but nervous. The heart rate was about 130 beats per minute and the blood pressure was unrecordable. Only the carotid and axillary pulses could be felt. She was resuscitated with rapid transfusions of blood and colloid.

Induction of anaesthesia proceeded with intravenous ketamine 50 mg, fentanyl 50 mg, and suxamethonium 75 mg to facilitate tracheal intubation. She was maintained with 100% oxygen and a bolus dose each of ketamine 10 mg and vecuronium 2 mg. Laparotomy

revealed neither active bleeding nor perforation of any viscus. There was bowel distension and fibrinous fluid in the peritoneal cavity. A diagnosis of primary peritonitis was made and the abdomen was closed. Intra-operatively, the patient was unstable. An axillary arterial line was inserted and revealed a systolic blood pressure of 60 to 70 mm Hg. Dopamine 10 µg/kg/min and adrenaline 0.8 µg/kg/min infusions were started. Despite the inotropic support, the patient remained hypotensive (<100 mm Hg systolic) and tachycardic. By then, she had become anuric and petechiae had appeared over the upper chest. A central venous line was inserted and revealed a pressure of 15 mm Hg. With these findings, her condition was diagnosed as septic shock with acute renal failure and possible disseminated intravascular coagulation. The patient was subsequently transferred to the intensive care unit.

At this point, the whole right thigh had become oedematous, with mottling. Large haemorrhagic bullae had formed and the skin was peeling (Fig 1). She was given ceftriaxone 1 g, gentamicin 80 mg, and metronidazole 500 mg. In the intensive care unit, oedema and mottling of the right thigh progressed rapidly over the next 2 hours and spread distally to the knee and calf. Vaginal examination was performed and was found to be normal. Following orthopaedic consultation, a diagnosis of toxic shock syndrome and necrotising fasciitis was suggested. Intravenous penicillin 2 mega-units and imipenem 1 g were given.

A balloon-tipped pulmonary arterial flotation catheter was inserted; the patient's haemodynamic profile indicated high cardiac output-low systemic vascular resistance syndrome. Additional inotropes—dobutamine 10 µg/kg/min and noradrenaline 0.1 µg/kg/min—were given. On the night of the laparotomy,

1a.



1b.



**Fig 1. Photographs of right leg/thigh showing progression of infection**  
(1a) oedema and large haemorrhagic bullae; (1b) skin peeling and muscle haemorrhage

the patient regained consciousness for about 1 hour. She could blink her eyes and maintain good hand-grip to commands. Peritoneal and right thigh swabs revealed a heavy growth of group A *S. pyogenes* that was sensitive to penicillin, ampicillin, ceftriaxone, and imipenem. Blood cultures, however, were negative.

On the second day following laparotomy, the patient's condition was poor; a decision was made to perform a fasciotomy on the right thigh and calf, since the soft tissue infection had become widespread and mottling had begun to appear on the left groin. Fasciotomy revealed extensive oedema with subcutaneous and muscle haemorrhage and petechiae, but there was no evidence of pus or gangrene. As the patient was unstable intra-operatively, minimal debridement was performed. Immunoglobulin 2.5 g and antibiotics were given. Plasmapheresis and hyperbaric oxygen were considered, but the patient was too ill to be transferred to a tertiary hospital. Following the fasciotomy, the patient remained critically ill, had an ongoing inotrope dependence, and developed adult respiratory distress syndrome, disseminated intravascular coagulation, and acute renal failure. Both legs were grossly oedematous and haemorrhaging. A change of wound dressing would have easily provoked haemodynamic instability.

On the following day, the patient suddenly developed irreversible shock. The lungs were almost impossible to ventilate, as the airway pressure and wedge pressure had escalated to more than 40 mm Hg and 30 mm Hg, respectively. There was massive generalised oedema and bleeding. Electrocardiography initially showed tachyarrhythmia and then idioventricular rhythm.

Despite aggressive resuscitation, the patient died on her eighth day of hospitalisation. As the family members were not keen to have a post-mortem examination of the patient performed, no autopsy was done.

## Discussion

Severe, invasive group A streptococcal (GAS) infections have been reported with increasing frequency from North America, Europe, Australia and Japan.<sup>4</sup> This case report is the first to describe fatal streptococcal TSLs in Singapore. This disease has attracted a great deal of attention because of its ability to cause explosive, often life-threatening disease. The onset of symptoms is typically acute and rapidly progressive over a period of 48 to 72 hours, as in the present case. It is frequently fatal even in immunocompetent patients. The overall mortality rate is approximately 30% despite aggressive medical and surgical intervention.<sup>5</sup> The case-fatality rate of severe GAS infections with necrotising fasciitis is between 20% to 50%,<sup>5</sup> whereas that of GAS myositis is between 80% to 100%.<sup>6</sup>

Although the clinical presentation of toxic shock due to *Staphylococcus aureus* and *S. pyogenes* are frequently similar, there are some distinguishing features (Box).<sup>7</sup> Group A streptococcal infections, for example, are associated with more extensive soft tissue infections, bullae formation, and bacteraemia. Hence, the term 'streptococcal toxic shock-like syndrome' is used in this case as opposed to 'staphylococcus toxic shock syndrome'. The soft tissue lesion, as described by Meleney,<sup>8</sup> frequently appears as only mild erythema in which heat and tenderness rapidly spread. During the next 1 to 2 days, the erythema darkens

### Comparison of toxic shock syndromes

	Staphylococcal infection	Streptococcal infection
Systemic signs; symptoms	Fever, myalgia, hypotension, diarrhoea, vomiting, thrombocytopenia, liver function abnormalities, increased creatine kinase and creatinine concentrations, proteinuria, pyuria, microscopic haematuria	Same as for staphylococcal infection
Skin/soft tissue/mucous membrane findings	Diffuse macular erythroderma with late desquamation, late onset erythematous pruritic maculopapular rash (>50% of cases), 'strawberry tongue', conjunctival haemorrhage, mucosal ulcerations	Desquamative macular erythroderma, bullae formation (5% of cases), associated soft-tissue infection (80% of cases), necrotising fasciitis or myositis (70%)
Diagnostic studies	Blood culture positive in <15% of cases; <i>Staphylococcus aureus</i> commonly isolated	Blood culture positive in >50% of cases
Antibiotic therapy	$\beta$ -Lactamase-resistant anti-staphylococcal antibiotic	Penicillin, erythromycin, vancomycin, clindamycin
Case fatality rate	<5%	30%

from red to purple and then blue; this is accompanied by the formation of blisters and bullae, and finally gangrene.<sup>8</sup> As we were unfamiliar with this presentation, we initially diagnosed the bluish hue on the patient's thigh as haematoma formation, secondary to intraperitoneal haemorrhage. Over the next 72 hours, however, the rapid clinical deterioration and cutaneous signs of this patient easily fitted the description of TSLS. As this patient had no other significant past medical history, we concluded that the cause of death was due to TSLS.

Historically, GAS infection is known to produce a wide range of clinical illnesses, from mild influenza-like infections to pneumonia, meningitis, peritonitis (as in this case), cellulitis, varicella-like lesions, and necrotising fasciitis. Despite these familiar traditional presentations, clinical features of TSLS have only been recognised because of two cases reported by Cone et al<sup>9</sup> in 1987. A number of patients describe prodromal influenza-like illness, fever and chills, but antecedent pharyngitis is rare. The patient in this case denied any of these symptoms preoperatively. The early spikes of fever (post-myomectomy) in this patient were probably the earliest signs of the disease. Pain, often in an extremity, is the most common initial symptom, even in the absence of any physical findings. In retrospect, we learned from the family that the patient did mention about pain in the right thigh before there were any signs present. Pain may also mimic symptoms associated with peritonitis, myocardial infarction, or pericarditis. The suspected portal of entry in many cases is the skin or mucous membranes. In this case, it appears that the intramuscular injection sites and/or abdominal incision could have been the portal of entry. In almost 50% of cases, however, a definite portal of entry is not found.<sup>5</sup> Suction lipectomy, hysterectomy, and vaginal delivery are other situations where infection is possible.<sup>5</sup> Rarely, the organism can be acquired through person-to-person contact.<sup>10</sup> Nasal and pharyngeal swabs of all our hospital staff were taken, but only one pharmacist tested positive. She had not come into contact with this patient, however.

Shock is usually apparent at the time of admission or within 4 to 8 hours in TSLS patients. The patient in this case deteriorated rapidly from American Society of Anaesthesiologists class I to V status within one morning. It is not uncommon that shock is refractory to volume expanders and inotropes. Renal involvement, manifested as raised creatinine levels, can be apparent at the time of admission, and between 48 and 72 hours thereafter, despite treatment. The first evidence of renal dysfunction in this patient was the initial pre-

laparotomy serum creatinine level of 212  $\mu\text{mol/L}$  (normal range, 50-110  $\mu\text{mol/L}$ ). Normal serum creatinine levels return within 4 to 6 weeks in those who survive TSLS.

Management of TSLS includes antibiotics, surgical debridement, and multi-organ support. Prompt antibiotic therapy is mandatory for an improved outcome. The first antibiotic given in this case was ampicillin, which is appropriate for GAS infection. The dosage was sufficient to treat cellulitis but was probably inadequate for necrotising fasciitis and myositis. Penicillin is indeed less effective against severe infections in which there is a large inoculum of streptococci. It has been suggested that the failure of penicillin in this setting is attributable to the slower multiplication rate of streptococci within the large inocula that are found in overwhelming sepsis, necrotising fasciitis, or myositis.<sup>11</sup> This may explain why this patient did not respond to the antibiotic therapy despite receiving four antibiotics to which the organism is sensitive. Other antibiotics available for the treatment of GAS infections are erythromycin, clindamycin, and ceftriaxone, all of which can be given to penicillin-allergic patients. Concerns have also been raised about the development of resistance to these agents. Other therapeutic modalities that remain to be evaluated include new antibiotics such as quinolones, monoclonal antitoxin antibodies, and receptor antagonists of tumour necrosis factor (TNF)  $-\alpha$  and interleukin 1.

In situations where GAS infection is well established, prompt surgical drainage, thorough debridement, fasciotomy, or even amputation may be necessary. In the present case, however, the extent of soft tissue involvement in the groin meant that amputation was not feasible.

The high mortality of TSLS underscores the need for a comprehensive understanding of the epidemiological features and pathogenesis of invasive GAS infections. This is a very rare postoperative complication and many physicians are not familiar with its initial signs and symptoms. It is imperative that clinicians become familiar with its presentation so that they can diagnose and treat it in a timely and effective manner.

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