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# Toxic shock syndrome secondary to Group A *Streptococcus* infection: A case report

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ABSTRACT

Toxic shock syndrome secondary to Group A *Streptococcus* infection is a rare but serious cause of women's morbidity and mortality which can easily be misdiagnosed. A 37-year-old woman presented to the emergency department in a state of shock after a two-day history of abdominal pain, fever, diarrhoea and green vaginal discharge. Following extensive investigations, she was proved to have septic shock secondary to Group A *Streptococcus pyogenes*. Despite receiving intravenous antibiotics, she required explorative laparotomy, which proceeded to subtotal hysterectomy and bilateral salpingectomy. Subsequently, she developed multi-organ failure, disseminated intravascular coagulation, and limb ischemia requiring below-knee amputation of the right limb. She was discharged home. The aim of this report is to raise the awareness about toxic shock syndrome from *Streptococcus pyogenes*. A high index of suspicion is required to promptly diagnose this rare yet potentially fatal infection.

## 1. Introduction

Group A *Streptococcus pyogenes* (GAS) is an anaerobic gram-positive coccus that causes a wide range of infections, [1] most commonly pharyngitis, tonsillitis, impetigo and cellulitis. Rarely, GAS can cause a severe and life-threatening infection, called invasive GAS. Toxic shock syndrome (TSS) is a severe and potentially fatal complication of invasive GAS. TSS constitutes a major burden to global morbidity and mortality [2]. This report discusses the case of a woman who presented with intractable shock and was diagnosed with TSS and multi-organ failure, who went on to develop limb ischemia that required amputation. The case highlights the merits of early diagnosis and timely intervention to manage TSS.

## 2. Case Presentation

A 37-year-old woman, morbidly obese and a heavy smoker, gravida 4 para 3–2, presented to the emergency department with a 2-day history of fever, vomiting, diarrhoea, green vaginal discharge as well as lower abdominal pain, oliguria for 24 hours, and shortness of breath. She has no history of diabetes, or cardiac or other illnesses. Her gynaecological history included hysteroscopy with dilatation and curettage for menorrhagia and laparoscopy with dye test for subfertility performed ten years previously. The patient had never had a cervical screening test. She had no past history of sexual transmitted disease.

On examination, the patient's heart rate was 130 beats/min, systolic blood pressure was 60 mmHg, temperature 36.5 °C, with cold lower limbs and detectable pulses. Chest and heart examinations were unremarkable but signs of acute abdomen were elicited on abdominal examination. General skin examination showed no signs of abrasions or inflammation. Vaginal examination was postponed because verbal consent for it was difficult to obtain given the woman's critical clinical condition.

Investigations revealed haemoglobin of 126 g/dL, white cell count of 24.3 × 10'/L, C-reactive protein of 348 mg/L, lactate of 12.3 mmol/L and creatinine of 407 mmol/L. Blood cultures were also sent. Chest X-ray was reported to be normal. Her abdominopelvic ultrasound and computed tomography scan were normal. She was commenced on broad-spectrum antibiotics, intravenous fluid and inotropes and oxygen. She was admitted to an intensive care unit under a multidisciplinary team for ongoing care.

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### 2.1. Outcome and Follow-Up

Despite of broad-spectrum antibiotics, oxygen, intravenous fluids, inotropes and corticosteroids her condition did not improve, so she underwent an explorative laparotomy which revealed hyperaemic uterus and tubes but no abscess was detected. No rectovaginal fistula was found on pelvic examination during the surgery. Vaginal and high cervical bacterial and sexual transmitted disease swabs were collected.

She continued to deteriorate, with multi-organ failure requiring dialysis for acute kidney failure. Therefore, a decision was made on the third post-operative day to proceed with a second laparotomy, during which she had subtotal hysterectomy and bilateral salpingectomy as the uterus was found to be necrotic. Histopathology results revealed ischemic necrosis of the uterus with haemorrhagic infarction, benign leiomyoma, adenomyosis and normal fallopian tubes. Blood culture results at this stage showed Group A *Streptococcus*, hence the patient was treated with intravenous clindamycin and benzyl penicillin. Subsequently, she developed compartment syndrome and digital necrosis in all 4 limbs (Figs. 1 and 2), requiring below-knee amputation of the right limb as well as partial amputation of other necrotic digits. She was discharged home after a prolonged hospital stay with outpatient follow-up at gynaecology and vascular clinics.

## 3. Discussion

Invasive Group A *Streptoccus pyogenes* (GAS) refers to invasion of GAS into the sterile sites of the body, including blood, lungs, central nervous system, bones or joints. It can lead to necrotising fasciitis, toxic shock syndrome and maternal sepsis during pregnancy or postpartum [1]. At a global level, invasive GAS has been reported to be a major cause of morbidity and mortality. The burden of disease is high, with an estimated 663,000 new cases and 163,000 deaths annually [2]. Higher incidence has been reported in winter and in developing countries. Infants and older persons seem to be at a higher risk for developing invasive GAS [3]. Importantly, one-third to one-fifth of cases have been reported in patients with no predisposing factors, as with the case reported here [3].

Toxic shock syndrome (TSS) is characterized by shock and multi-organ failure. It results from release of inflammatory cytokines by streptococcal toxins resulting in capillary leak and tissue damage. It occurs in about one-third of invasive GAS cases, with an associated mortality of 33–81 % [4]. The Centers for Disease Control and Prevention defines the diagnostic criteria for TSS by presence of hypotension, multi-organ failure and any two of the following: renal impairment, liver involvement, coagulopathy, acute respiratory distress syndrome, generalised erythematous rash and soft-tissue necrosis, such as myositis, gangrene and necrotizing fasciitis. The diagnosis is confirmed by isolation of GAS from a sterile site such as blood, pericardial, joint, pleural and cerebrospinal fluid [3,5]. The case reported here meets most of these diagnostic criteria.

**Fig. 1.** Ischemia of upper limb secondary to group A *Streptococcus pyogenes* toxic shock syndrome.

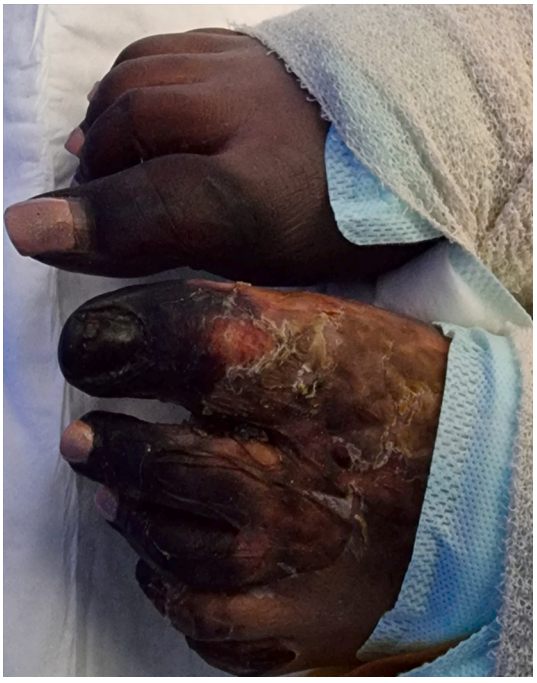

**Fig. 2.** Ischemia of lower limb secondary to group A *Streptococcus pyogenes* toxic shock syndrome.

Invasive GAS infection in obstetrics and gynaecology has been widely reported. The incidence of GAS is 20 % higher among pregnant women than among non-pregnant women. A death has been reported of a 16-year-old girl at 37 weeks of gestation due to invasive GAS TSS [6]. TSS induced by invasive GAS infection during pregnancy can have adverse fetal outcome. A case of fetal death in utero at 31 weeks of gestation secondary to acute respiratory distress syndrome has been reported [7]. In a nationwide study that analysed maternal 15 deaths and 13 surviving patients with TSS due to invasive GAS, the number of fetal deaths was higher in the maternal deaths group than in the surviving group [8]. GAS in the immediate post-partum period (up to day 4) has a high mortality rate, of up to 60 %. Invasive GAS can result in endometritis in post-partum women and most of the reported cases have been after uncomplicated vaginal delivery [9]. There have been reported cases of TSS secondary to an intra-uterine contraceptive device, gynaecological laparoscopies, gynae-radiological procedures like hystrosalpingo-contrast sonography and tampon use [10–13].

Management of GAS-induced TSS requires a multidisciplinary team, including infectious disease specialists, intensivists, surgeons and microbiologists. Close observation in a high-dependency unit with intubation and aggressive early resuscitation with large-volume crystalloids and vasopressors is paramount for maintenance of adequate perfusion and organ survival. Penicillin G remains the first-line treatment for GAS-induced TSS. Antibiotics such as vancomycin or clindamycin need to be used in combination with penicillin as they have the ability to inhibit protein synthesis and hence block the production of exotoxins from GAS [14,15], as in the reported case. It is of extreme importance to keep in mind that antibiotic penetration into infected and necrotic tissues is low, if not absent, as a result of poor vascularization secondary to infection-induced microvascular thrombosis. Surgical debridement of necrotic tissues is the only way to enhance antibiotic penetration into those areas and reduce mortality. Intravenous immunoglobulins (IVIG) have also been considered as an adjuvant therapy in the management of GAS-induced TSS [3]. Few investigators have studied the role of IVIG in

reducing mortality in TSS cases. The postulated mechanisms of action of IVIG in such cases are neutralization of GAS toxins, possible immunomodulation, and improvement in bacterial phagocytosis and opsonisation. However, there is no consensus on a recommendation for the routine use of IVIG in GAS-induced TSS cases. More research is required.

## 4. Conclusions

Toxic shock syndrome induced by Group A *Streptococcus pyogenes* is a rare but potentially life-threatening condition. Shock and multi-organ failure can rapidly develop and progress in a short period. A high index of suspicion and awareness are required for early identification and appropriate management. Multidisciplinary team involvement is necessary for management, including aggressive resuscitation, as well as medical and surgical treatment. Mortality and long-term morbidity rates are high. Survival can be at the cost of living with lifelong morbidity secondary to necrosis and ischemia as well as undesirable outcomes like amputation.

### *Contributors*

Lara Strakian contributed to the conception of the case report, acquisition of data, analysis and interpretation of data, and drafted the article.

Sonal Karia contributed to patient care, conception of the case report, acquisition of data, and critical revision of the article for important intellectual content.

Both authors approved of the final submitted manuscript.

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### *Conflict of interest statement*

The authors declare that they have no conflict of interest regarding the publication of this case report.

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