

# A Case Report of Streptococcus Dysgalactiae Toxic Shock Syndrome Complicated with Symmetric Peripheral Gangrene

Xiaoqing Shen\*, Hongkai Liang\*, Guishen Wu, Miaolian Chen, Jianwei Li

Department of Critical Care Medicine, Zhongshan People's Hospital, Zhongshan, People's Republic of China

\*These authors contributed equally to this work

Correspondence: Jianwei Li, Department of Critical Care Medicine, Zhongshan People's Hospital, Zhongshan, 528400, People's Republic of China, Email [lijwprof2005@163.com](mailto:lijwprof2005@163.com)

**Abstract:** *Streptococcus dysgalactiae subspecies equisimilis* (SDSE) is considered an important bacterial pathogen, and attention has also increased with the increasing number of invasive SDSE infections. Here, we report a patient with *S. dysgalactiae* toxic shock syndrome complicated by symmetrical peripheral gangrene (SPG). Despite surviving active treatment, amputation severely impacts the quality of life of patients. Therefore, we should pay attention to the early treatment of SDSE infection and the prevention and treatment of related complications.

**Keywords:** *Streptococcus dysgalactiae subspecies equisimilis*, streptococcal poisoning shock syndrome, symmetric peripheral gangrene

## Introduction

*Streptococcus dysgalactiae subspecies equisimilis* (SDSE) belongs to a group of  $\beta$ -hemolytic streptococci, and is a common symbiont of humans. It is often colonizes in the human throat, skin, gastrointestinal tract, and the vagina.<sup>1</sup> The incidence of bacteremia caused by SDSE is increasing worldwide, and streptococcal toxic shock syndrome (STSS) is of particular concern.

Symmetric peripheral gangrene (SPG) is a rare and serious complication of septic shock associated with a high amputation rate and mortality. It is a symmetrical, distal ischemic injury in the absence of major vascular occlusive diseases.<sup>2</sup> Herein, we report a case of STSS caused by a SDSE infection that was complicated by rapidly progressive SPG that involved the toes and fingers.

## Case Report

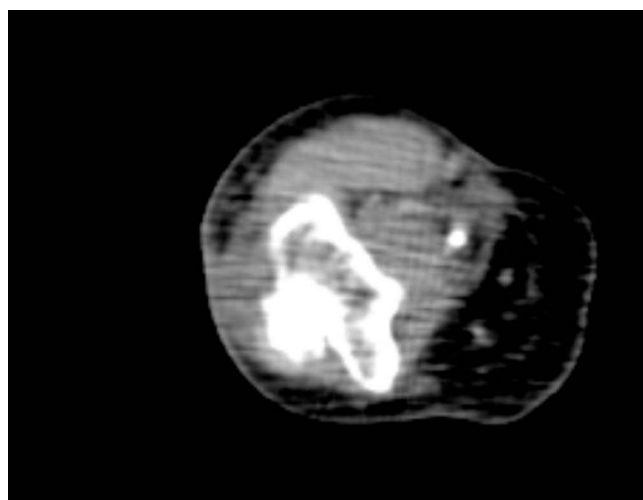
A 69-year-old woman was diagnosed as having right breast cancer in 2015 and underwent radical surgery. In 16 August 2022, she developed high fever, pain and swelling in her right upper limb. After 4 days of treatment in Zhongshan Huangpu Hospital her symptoms became worse and she was transferred to the intensive care unit (ICU) of Zhongshan People's Hospital due to septic shock. She was confused on admission, The examination showed a blood pressure of 80/40 mmHg (100–140/60–90mmHg), a heart rate of 105 beats/min (60–100 beats/min), a breathing frequency of 25 breaths/min (12–20 breaths/min), an armpit temperature of 39°C (36–37°C), and a peripheral oxygen saturation of 94% (95–100%). Laboratory studies revealed white blood cell (WBC) count was  $1.17 \times 10^9/L$ , platelet count was  $70 \times 10^9/L$ , hemoglobin was 94 g/L (all decreased), and 85.5% neutrophils, interleukin-6 (IL-6) > 5000 pg/mL, C-reactive protein (CRP) was 164.0 mg/L. Serum creatinine was elevated at 158  $\mu\text{mol/L}$  (Table 1). Enhanced spiral Computed tomography (CT) of the right upper limb showed mild edema of the upper arm and forearm (Figure 1). Vascular color ultrasound of extremities normal.

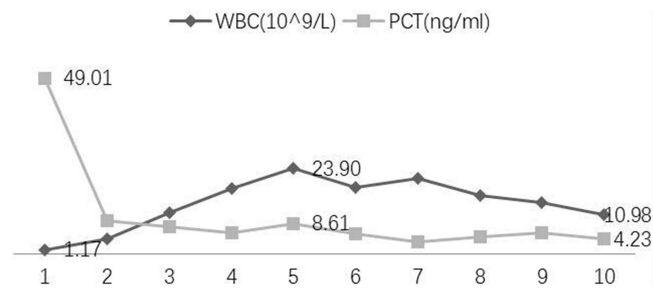
**Table 1** Laboratory Data at Hospital Admission

Hematological Parameter	Value	Reference Range
WBC	1.17 *10 <sup>9</sup> /L	3.69–9.16 (10 <sup>9</sup> /L)
Neutrophils	85.5%	50.0–70.0 (%)
Eosinophils	7.7%	0.5–5.0 (%)
Basophils	0%	0–1.00 (%)
Hemoglobin	94 g/L	113–151 (g/L)
Platelets	70 *10 <sup>9</sup> /L	101–320 (10 <sup>9</sup> /L)
Procalcitonin	49.21 ng/mL	0–0.05 (ng/mL)
CRP	164 mg/L	0–5.0mg/L
IL-6	>5000 pg/mL	0–7.00 (pg/mL)
CK	323 U/L	41–186 (U/L)
CK-MB	26 U/L	0–24 (U/L)
Cr	158 umol/L	45–84 (umol/L)
BUN	16.93 mmol/L	2.9–8.2 (mmol/L)
ALT	35 U/L	7–40 (U/L)
AST	89 U/L	13–35 (U/L)
Total protein	58.8 g/L	65.0–85.0 (g/L)
PT	12.8 s	9.0–12.5 (s)
APTT	33.2 s	25.2–38.5 (s)
Fibrinogen	4.61g/L	2.0–4.0 (g/L)

**Abbreviations:** WBC, white blood cell count; CRP, C-reactive protein; IL-6, Interleukin-6; CK, creatine kinase; CK-MB, Creatine kinase isoenzyme; Cr, creatinine; BUN, Blood urea nitrogen; ALT, alanine aminotransferase; AST, aspartate aminotransferase; PT, prothrombin time; APTT, activated partial thromboplastin time.

Considering the soft tissue infection of the right upper limb complicated with septic shock, empirical meropenem (1g, q8h) combined with vancomycin (1g, q12h) via intravenous drip for anti-infection, and norepinephrine was given to maintain an average arterial blood pressure of > 65 mmHg. In order to obtain relevant results as soon as possible, blood samples were submitted for metagenomic next-generation sequencing (mNGS) testing before starting antibiotic use, while traditional blood cultures, sputum cultures, and urine cultures were perfected. Other treatments included rehydration, low-molecular-weight heparin for anticoagulation, drugs for raising platelets and topical magnesium sulfate on the right upper limb. On the second day of treatment, the patient's procalcitonin decreased to 9.47 pg/mL (Figure 2). The mNGS results indicated the presence of SDSE. However, the patient developed cyanosis of her fingers and toes, large

**Figure 1** Spiral enhanced computer scan of right arm showed mild edema.

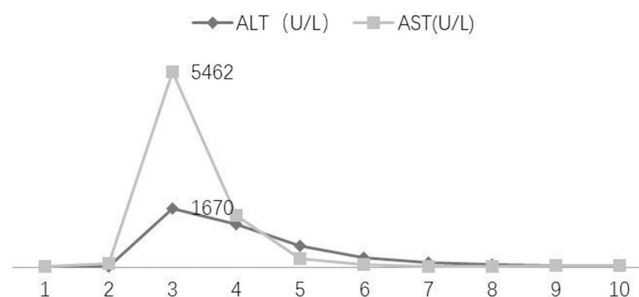


**Figure 2** Changes of white blood cell (WBC) count and procalcitonin (PCT) indicators in intensive care unit.

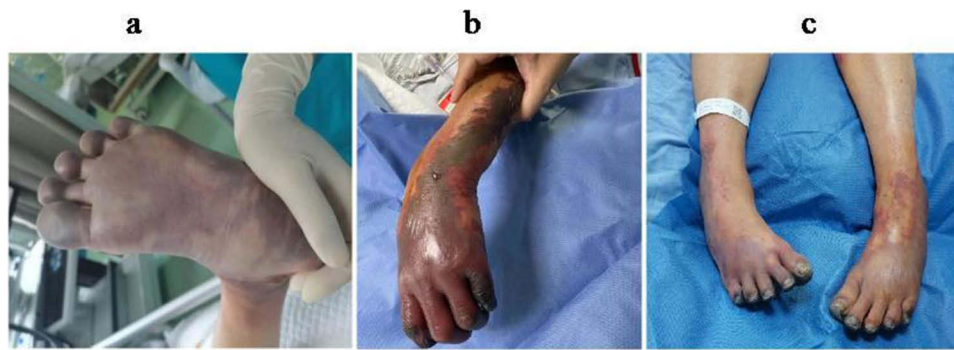
purpura on the skin, and some large blisters (Figure 3a–c). Liver function tests on day 3 showed a steep rise in transaminases (Figure 4) and progression of limb end ischemia was observed (Figures 5a–c), while blood cultures also showed SDSE. *Streptococcus* was isolated from blood, combined with hypotension, multiple organ dysfunction (including coagulation, liver function, renal function), blister formation, and limb gangrene, and in summary, the patient's symptoms and laboratory data met the criteria for STSS. The results of drug sensitivity showed that the patient was sensitive to penicillin, ceftriaxone, linezolid and vancomycin, and intermediate to clindamycin. However, because the patient had a history of allergy to penicillin he also had renal impairment and thrombocytopenia. In order to avoid further aggravation of renal insufficiency and thrombocytopenia, we chose intravenous drip of ceftriaxone (2g qd) for anti-infection, and anisodamine was added to improve microcirculation in an attempt to reduce acral ischemia. After 10 days of treatment, the patient was transferred from the ICU to the general ward. However, the ischemia at the extremities gradually worsened and amputation was performed after eventually developed SPG (Figure 6a–c).



**Figure 3** Characteristic features of *Streptococcal* Infected Limbs.  
**Notes:** (a) Limb ischemia. (b) Subcutaneous haemorrhage. (c) Giant blisters.



**Figure 4** Changes in transaminase parameters in the intensive care unit.  
**Abbreviations:** ALT, Alanine Aminotransferase; AST, Aspartate Aminotransferase.



**Figure 5** Limb ischemia following SDSE infection.

**Notes:** (a) Lower limb ischemia. (b) Upper limb ischemia. (c) Symmetrical limb ischemia.



**Figure 6** Manifestations of SPG Following SDSE Infection.

**Notes:** (a). Gangrene plantaris. (b) Gangrene dorsalis pedis. (c). Upper limb gangrene.

## Discussion

SDSE (group C or G Streptococcus) belongs to the hemolytic Streptococcus type B family. Group C and group G Streptococci are also commonly called pyogenic Streptococci because they are genetically close to pyogenic Streptococci.<sup>3</sup> Because SDSE was recognized as a part of the normal flora of the human pharynx, skin, gastrointestinal tract, and vagina,<sup>4,5</sup> the colonization of these bacteria has been considered harmless. However, the pathogenicity of SDSE is currently well recognized, and an increasing number of epidemiological studies have indicated that it can cause a variety of diseases similar to those caused by Streptococcus pyogenes. Notably, the number of invasive SDSE infections is reported to be increasing world-wide,<sup>6–9</sup> and STSS and bacteremia are of particular concern.<sup>10–14</sup> It has also been noted that the incidence of bacteremia is gradually increasing.<sup>15,16</sup> However, no large-scale epidemiological studies in China have provided data on SDSE infection. Many studies have found that invasive SDSE infection is more commonly seen as a community-acquired disease in elderly patients with comorbidities.<sup>17–19</sup> As the number of elderly people in China is increasing, infection with the invasive Streptococcus dysgalactiae subsp. equisimilis is also likely increase and should attract the attention of clinicians.

The patient reported herein was an elderly woman with a history of breast cancer. Thus, she was at high-risk for invasive SDSE infection, and eventually developed SDSE-induced STSS, and most previous STSS cases were caused by GAS and progressed rapidly with a mortality rate of more than 50%, while in recent years, GCS has also been shown to be one of the main pathogens causing various infectious diseases, and most STSS patients associated with GCS and GGS have underlying diseases such as cardiopulmonary disease, diabetes, malignancy, and renal or hepatic failure.<sup>20</sup> In particular, in GGS, SDSE is considered to be the organism causing non-GAS type STSS, and in patients with systemic infections caused by GAS, the incidence of STSS is about 7%, which is higher than that of STSS caused by GGS.<sup>21</sup> Antibiotic treatment is necessary for SDSE. SDSE and other large colony C and G Streptococci are usually sensitive to

penicillin, which is considered the first choice for the treatment of infections caused by these microorganisms. In our patient, because the patient was allergic to penicillin, we chose ceftriaxone for anti-infection, along with appropriate supportive measures (including fluid resuscitation, administration of vasopressors, and mechanical ventilation), and the patient eventually obtained a favorable outcome. Most cases of STSS are caused by GAS. Among patients with STSS, those with group A Streptococci infection who receive intravenous immunoglobulin (IVIG) have improved outcomes.<sup>22</sup> However, there is still a lack of research regarding SDSE infection.

Notably, our patient rapidly developed SPG during the disease progression. SPG can be secondary to many conditions such as sepsis and heart failure, and it typically involves the distal limbs but can also involve the nose, lips, ears, scalp, and genitals. It is often aggravated by factors including warfarin treatment, deep vein thrombosis, hypotension, pressor drug treatment, and anticoagulation system failure.<sup>23–27</sup> Recently, acute ischemic hepatitis has been identified as a potential risk factor for symmetric peripheral gangrene,<sup>28,29</sup> and may be related to impairment of protein C synthesis caused by acute liver dysfunction. About a quarter of patients with SPG will require amputation, and the condition is associated with a mortality rate of over 50%. Only a few cases of SPG have been reported, and little is known about its epidemiology. Our patient received anticoagulation treatment after diagnosis, but cyanosis appeared at the distal limbs on the second day and progressed despite the anticoagulation treatment. During her hospital course, hypotension, use of vasoactive drugs, and liver dysfunction may have aggravated the ischemia, eventually leading to the development of SPG. This kind of ischemic limb injury can occur rapidly, and even if anticoagulant therapy is begun immediately after the ischemia is recognized it may have not effect.

## Conclusion

We reported a case of SDSE-induced STSS complicated with symmetric peripheral gangrene. This case highlights that more attention should be given to pathogenic SDSE infections, and the potential for progression to SPG.

## Ethics Approval and Consent

The design and methods of the research are in accordance with the requirements of related regulations and procedures as well as the ethical principles. The study approved by the Ethical Committee of Zhongshan People's Hospital (Medical Ethics 2023-009). The patient information in this article is anonymous and written informed consent was obtained from the patient's immediate family for the publication of this case report and accompanying images.

## Consent for Publication

Written informed consent was obtained from the patient's immediate family for the publication of this case report and accompanying images. A copy of the written consent form is available for review by the Editor-in-Chief of this journal. All authors read and approved the final manuscript.

## Acknowledgments

We would like to thank the members of our department for their insight and support. Xiaoqing Shen and Hongkai Liang are co-first authors for this study.

## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work. All authors have read and approved the manuscript.

## Funding

No funding was received for this study.



## Disclosure

The authors declare that they have no conflicts of interests.

## References

- Baracco GJ, Fischetti VA, Novick RP, Ferretti JJ, Portnoy DA, Rood JJ.; Infections Caused by Group C and G Streptococcus (*Streptococcus dysgalactiae* subsp. *equisimilis* and others): epidemiological and clinical aspects. *Microbiol Spectr*. 2019;7(2). doi:10.1128/microbiolspec.GPP3-0016-2018
- Sharma BD, Kabra SR, Gupta B. Symmetrical peripheral gangrene. *Trop Doct*. 2016;34(1):2–4. doi:10.1177/004947550403400102
- Jensen A, Kilian M. Delineation of *Streptococcus dysgalactiae*, its subspecies, and its clinical and phylogenetic relationship to *Streptococcus pyogenes*. *J Clin Microbiol*. 2012;50(1):113–126. doi:10.1128/JCM.05900-11
- Auckenthaler R, Hermans P, Washington J. Group G streptococcal bacteremia: clinical study and review of the literature. *Rev Infect Dis*. 1983;5(2):196–204. doi:10.1093/clinids/5.2.196
- Liao C-H, Liu L-C, Huang Y-T, Teng L-J, Hsueh P-R. Bacteremia caused by group G streptococci, Taiwan. *Emerg Infect Dis*. 2008;14(5):837. doi:10.3201/eid1405.070130
- Hughes JM, Wilson ME, Brandt CM, Spellerberg B. Human infections due to *Streptococcus dysgalactiae* subspecies *equisimilis*. *Clin Infect Dis*. 2009;49(5):766–772. doi:10.1086/605085
- Barnham M, Kerby J, Chandler R, Millar M. Group C streptococci in human infection: a study of 308 isolates with clinical correlations. *Epidemiol Infect*. 1989;102(3):379–390. doi:10.1017/S0950268800030090
- Gustafson LW, Blaakær J, Helmig RB; Group A streptococci infection. A systematic clinical review exemplified by cases from an obstetric department. *Eur J Obstet Gynecol Reprod Biol*. 2017;215:33–40. doi:10.1016/j.ejogrb.2017.05.020
- Broyles LN, Van Beneden C, Beall B, et al. Population-based study of invasive disease due to  $\beta$ -hemolytic streptococci of groups other than A and B. *Clin Infect Dis*. 2009;48(6):706–712. doi:10.1086/597035
- Efstratiou A. Pyogenic streptococci of Lancefield groups C and G as pathogens in man. *J Appl Microbiol*. 1997;83(S1):72S–79S. doi:10.1046/j.1365-2672.83.s1.8.x
- Loubinoux J, Plainvert C, Collobert G, Touak G, Bouvet A, Poyart C. Adult invasive and noninvasive infections due to *Streptococcus dysgalactiae* subsp. *equisimilis* in France from 2006 to 2010. *J Clin Microbiol*. 2013;51(8):2724–2727. doi:10.1128/JCM.01262-13
- Kittang B, Bruun T, Langeland N, Mylvaganam H, Glambek M, Skrede S. Invasive group A, C and G streptococcal disease in western Norway: virulence gene profiles, clinical features and outcomes. *Clin Microbiol Infect*. 2011;17(3):358–364. doi:10.1111/j.1469-0691.2010.03253.x
- Oppegaard O, Mylvaganam H, Skrede S, Langeland N, Kittang B. Sequence diversity of *sicG* among group C and G *Streptococcus dysgalactiae* subspecies *equisimilis* isolates associated with human infections in western Norway. *Eur J Clin Microbiol Infect Dis*. 2014;33:273–277. doi:10.1007/s10096-013-1955-0
- Rantala S. *Streptococcus dysgalactiae* subsp. *equisimilis* bacteremia: an emerging infection. *Eur J Clin Microbiol Infect Dis*. 2014;33:1303–1310. doi:10.1007/s10096-014-2092-0
- Pérez-Ayala A, Pérez-Molina J, Norman F, et al. Chagas disease in Latin American migrants: a Spanish challenge. *Clin Microbiol Infect*. 2011;17(7):1108–1113. doi:10.1111/j.1469-0691.2010.03423.x
- Oppegaard O, Mylvaganam H, Kittang B. Beta-haemolytic group A, C and G streptococcal infections in Western Norway: a 15-year retrospective survey. *Clin Microbiol Infect*. 2015;21(2):171–178. doi:10.1016/j.cmi.2014.08.019
- Ekelund K, Skinshøj P, Madsen J, Konradsen H. Invasive group A, B, C and G streptococcal infections in Denmark 1999–2002: epidemiological and clinical aspects. *Clin Microbiol Infect*. 2005;11(7):569–576. doi:10.1111/j.1469-0691.2005.01169.x
- Takahashi T, Sunaoshi K, Sunakawa K, et al. Clinical aspects of invasive infections with *Streptococcus dysgalactiae* ssp. *equisimilis* in Japan: differences with respect to *Streptococcus pyogenes* and *Streptococcus agalactiae* infections. *Clin Microbiol Infect*. 2010;16(8):1097–1103. doi:10.1111/j.1469-0691.2009.03047.x
- Takahashi T, Asami R, Tanabe K, et al. Clinical aspects of invasive infection with *Streptococcus dysgalactiae* subsp. *equisimilis* in elderly patients. *J Infect Chemother*. 2010;16(1):68–71. doi:10.1007/s10156-009-0016-1
- Hashikawa S, Iinuma Y, Furushita M, et al. Characterization of group C and G streptococcal strains that cause streptococcal toxic shock syndrome. *J Clin Microbiol*. 2004;42(1):186–192. doi:10.1128/JCM.42.1.186-192.2004
- Takahashi T, Ubukata K, Watanabe H. Invasive infection caused by *Streptococcus dysgalactiae* subsp. *equisimilis*: characteristics of strains and clinical features. *J Infect Chemother*. 2011;17(1):1–10. doi:10.1007/s10156-010-0084-2
- Kaul R, McGeer A, Norrby-Teglund A, et al. Intravenous immunoglobulin therapy for streptococcal toxic shock syndrome—a comparative observational study. *Clin Infect Dis*. 1999;28(4):800–807. doi:10.1086/515199
- Warkentin TE, Cook RJ, Sarode R, Sloane DA, Crowther MA. Warfarin-induced venous limb ischemia/gangrene complicating cancer: a novel and clinically distinct syndrome. *Blood J Am Soc Hematol*. 2015;126(4):486–493.
- Warkentin TE, Elavathil LJ, Hayward CP, Johnston MA, Russett JI, Kelton JG. The pathogenesis of venous limb gangrene associated with heparin-induced thrombocytopenia. *Ann Intern Med*. 1997;127(9):804–812. doi:10.7326/0003-4819-127-9-199711010-00005
- Molos MA, Hall JC. Symmetrical peripheral gangrene and disseminated intravascular coagulation. *Arch Dermatol*. 1985;121(8):1057–1061. doi:10.1001/archderm.1985.01660080111027
- Ghosh S, Bandyopadhyay D, Ghosh A. Symmetrical peripheral gangrene: a prospective study of 14 consecutive cases in a tertiary-care hospital in eastern India. *J Eur Acad Dermatol Venereol*. 2010;24(2):214–218. doi:10.1111/j.1468-3083.2009.03329.x
- Warkentin TE. Ischemic limb gangrene with pulses. *N Engl J Med*. 2015;373(7):642–655. doi:10.1056/NEJMra1316259
- Warkentin TE. Anticoagulant failure in coagulopathic patients: PTT confounding and other pitfalls. *Expert Opin Drug Saf*. 2014;13(1):25–43. doi:10.1517/14740338.2013.823946
- Warkentin TE. Heparin-induced thrombocytopenia in critically ill patients. In: *Seminars in Thrombosis and Hemostasis*. Thieme Medical Publishers; 2015:049–060.

Infection and Drug Resistance

Dovepress

### Publish your work in this journal

Infection and Drug Resistance is an international, peer-reviewed open-access journal that focuses on the optimal treatment of infection (bacterial, fungal and viral) and the development and institution of preventive strategies to minimize the development and spread of resistance. The journal is specifically concerned with the epidemiology of antibiotic resistance and the mechanisms of resistance development and diffusion in both hospitals and the community. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <https://www.dovepress.com/infection-and-drug-resistance-journal>