SAGE Open Medical Case Reports
Volume 11: 1–6

DOI: 10.1177/2050313X231207202
journals.sagepub.com/home/sco
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Streptococcal toxic shock syndrome with associated necrotising fasciitis necessitating amputation of the lower extremity – A case report

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Abstract

Streptococcal toxic shock syndrome is a severe, invasive and life-threatening infection associated with a high risk of rapid multiorgan failure. It is associated with high morbidity and mortality. Streptococcal toxic shock syndrome is very commonly caused by group A-*Streptococcus pyogenes*, ß-haemolytic streptococcus, a typical human-specific gram-positive bacterial pathogen. We present here the case report of a 54-year-old man with a rapidly progressive streptococcal toxic shock syndrome due to necrotising fasciitis of the left lower limb and describe the successful treatment through close interdisciplinary care.

Keywords

Streptococcal toxic shock syndrome, necrotising fasciitis, β-haemolytic streptococcus, group A-*Streptococcus pyogenes*, computer tomography, amputation

Date received: 24 June 2023; accepted: 26 September 2023

Introduction

Necrotising fasciitis is a severe disease caused, among other things, by invasive infections with ß-haemolytic streptococcus. The most important representative is *Streptococcus pyogenes* which is also classified as group A streptococcus (GAS). Typically, multiple skin layers are rapidly and progressively infiltrated by inflammatory cells, leading to streptococcal toxic shock syndrome (STSS).[1,2]

STSS usually leads to a rapid deterioration in the clinical condition of patients with multiple organ failure with symptoms of pain, fever, sepsis and disseminated intravascular coagulation[3,4] and is associated with a very adverse prognosis and mortality rates of about 5%–10% in children and 30%–80% in adults.[5,6] STSS is based on a combination of the effect of streptococcal enterotoxins with superantigen activity and the host response to streptococcal infection, although the exact mechanism of STSS is not fully understood.[7] Management of invasive group A streptococcal infections usually requires admission to the intensive care unit (ICU) and interdisciplinary treatment of various organ dysfunctions.[8]

Several clinical and experimental studies have shown that treatment with penicillin, clindamycin and immunoglobulins can reduce morbidity and mortality in patients with STSS.[9]

The aim of this case report is to describe the complex clinical presentation of STSS, highlight therapeutic options, illuminate different treatment pathways and present a successful outcome as a lighthouse case to help other medical professionals decide on the choice of therapy after a full investigation (including laboratory chemistry, microbiology

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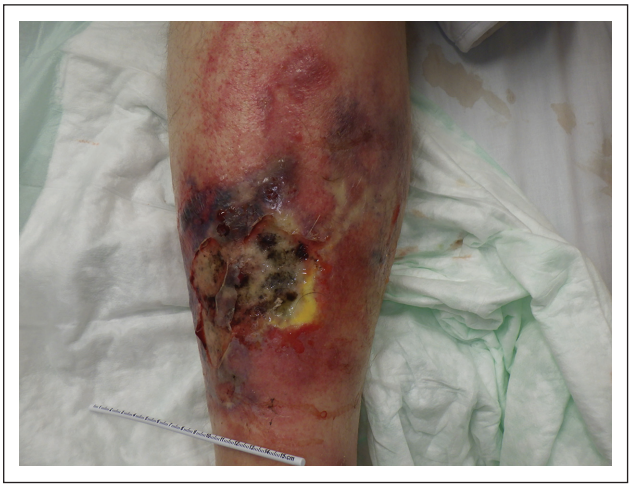

Figure 1. At admission, the patient presented with a very rapidly worsening swelling of the left lower leg with already partially necrotic areas.

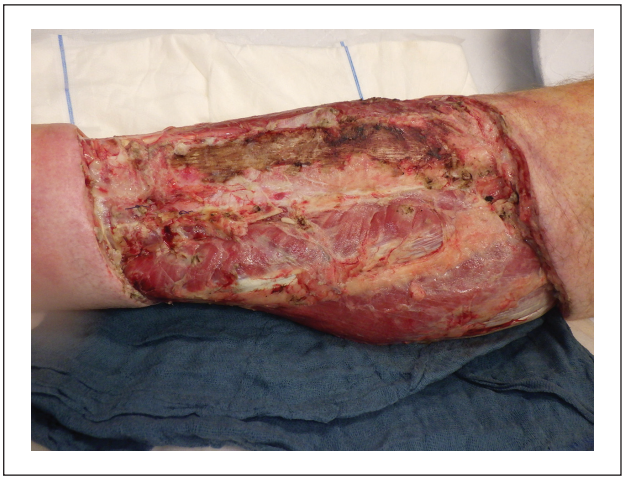

Figure 2. Wound debridement and fasciotomy were performed at the right lower leg. This photograph was taken after the procedure on the first day after admission to the intensive care unit.

and radiology). In this context, the present case report confirms the already known newer literature, adapts it to the clinical context and emphasises the rapid and time-critical interdisciplinary clinical cooperation.

Case

A 54-year-old Caucasian male was admitted to the emergency department of our hospital by his general practitioner in the evening. The patient had been experiencing progressive pain and swelling of the right lower extremity with permanent redness and petechial haemorrhage for a week (Figure 1), both of which had worsened extremely since the morning. By his own account, he had hit his leg in the last week without remembering when exactly this had happened. For most of the time, the patient avoided going to the physician and showed a lack of understanding. Due to his poor condition, increasing pain and at the urging of his relatives, he now underwent medical treatment for the first time in many years. For this reason, the patient was not known to have any previous illnesses.

Day of admission, first day

At the time of admission to the emergency department, he was in septic shock with tachycardia, dyspnoea and arterial hypotension, requiring immediate transfer (30 min after arrival in the emergency department) to the interdisciplinary surgical ICU. Physical examination revealed the following values: blood pressure 81/42 mmHg, heart rate 128 beats per minute (bpm), temperature 39.2°C, respiratory rate 38 breaths per minute and SpO_2 96% on 6 L/min of oxygen via a breathing mask, with a paO_2 of 114 mmHg. Transthoracic echocardiography revealed a moderately impaired left ventricular ejection fraction of 40%, well-functioning heart valves, no endocarditis and no pericardial effusion. The first laboratory values after admission to the ICU were as follows: a severely elevated white blood cell count of 20.23×10^9/L, a very high elevated C-reactive protein (CRP) of 3362 nmol/L and an extremely elevated procalcitonin (PCT) level of 43.5 µg/L.

Lactate was also elevated at 8.8 mmol/L, and platelet count was 160×10^9/L. Total bilirubin was slightly elevated at 42.75 µmol/L, aspartate aminotransferase was 950 nmol/s*L and alanine aminotransferase was 850 nmol/s*L. Although the patient did not report diabetes mellitus in his medical history, a blood glucose level of 20.8 mmol/L was detected on admission, indicating long-standing, undiagnosed and untreated diabetes mellitus.

Due to the rapidly spreading ulcerations on the lower leg, necrotising fasciitis was quickly suspected clinically as the cause of the severe septic event.

During the stay in the ICU, severe sepsis with multiple organ failure developed. In addition to liver failure, renal failure occurred with elevated renal values (creatinine 382 µmol/L, urea 18.8 mmol/L) and absent urine output in terms of acute renal failure. In addition, the myoglobin level increased to 125 nmol/L. Continuous veno-venous haemodialysis under calcium-citrate anticoagulation was started on the day of admission. Initially, continuous haemodialysis was required for 8 days, followed by discontinuous dialysis for an additional week. Afterwards, the kidney function recovered.

As a result of the septic event, the patient became somnolent. A score of −2 on the Richmond Agitation and Sedation Scale[10] was obtained, resulting in the patient being intubated 2 h after arrival in the ICU. The first blood gas analysis after intubation showed acidosis with a paO_2 of 179 mmHg at a FiO_2 of 70%, resulting in a Horowitz Index[11,12] of 256 mmHg, corresponding to mild acute respiratory distress syndrome (ARDS).

6 h after arrival in the ICU, the patient was taken to the operating room, where extensive wound debridement,

excision of the fascia (Figure 2) and microbiological biopsy sampling were performed.

Second day

On the first postoperative day, the patient's haemodynamic situation deteriorated significantly despite excessive volume (4 L of crystalloids) and catecholamine (1.2 mg/h norepinephrine) therapy. Therefore, a whole-body computed tomography (CT) scan was performed for further focus search. These CT scans showed an elongated subcutaneous fluid retention of the right thigh down to the level of the upper ankle with small air bubbles along the fascia of the medial head of the gastrocnemius muscle (Figure 3).

Due to the clinical deterioration and the CT findings, the indication for immediate transfemoral amputation was given. At this time, the catecholamine requirement increased and was already 1.6 mg/h of norepinephrine. The inflammatory signs had increased to the following values at this time: Temperature, 39.1°C; leukocytes, 25.8×10^9/L; CRP, 4067 nmol/l; PCT, 60.40 µg/L; IL-6, 2532 U/L; lipopolysaccharide-binding protein (LBP), 91 U/L; and HLA-DR, 27.3%.

The amputation was performed on the same day. A stump revision became necessary on the fourth day after hospital admission, and with proper surgical care, the wound could be finally closed on the ninth day after hospitalisation. Pathologic findings confirmed severe necrotising florid inflammation consistent with necrotising fasciitis (Figure 4).

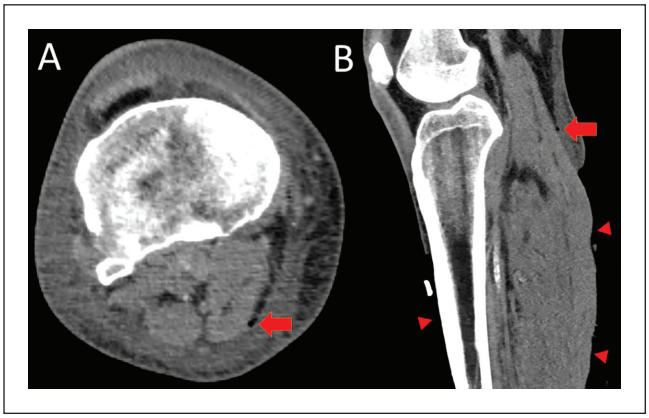

Figure 3. Computer tomography of the right knee and lower leg: (a) axial view and (b) sagittal view. Note the perifascial air along the gastrocnemius muscle (arrow) and the large circumferential skin defects (arrowhead).

Antibiotic and immunological therapy

Depending on the microbiological findings, the anti-infective therapy was adjusted several times. Immediately after admission, empiric antimicrobial therapy with intravenous piperacillin/tazobactam 4×4.5 g/day was initiated. This was immediately extended by the intravenous administration of Clindamycin 3×900 mg/day in order to be able to treat a possible infection with *Clostridium perfringens* at an early stage in the ICU. When *Streptococcus pyogenes* was detected in the wound swab and blood cultures on the second day after admission, antibiotic therapy with piperacillin/tazobactam was changed to intravenous penicillin G 4×5 million I.U./day according to the antibiogram. Clindamycin was administered unchanged.

During continuous dialysis treatment, the use of a high-capacity filter was avoided because immunoglobulin therapy was started at the same time as dialysis treatment due to the limited time slot in the patient's critical condition.

The effect of antibiotic levels was monitored during renal replacement procedures by close drug monitoring. The immunological defence competence was severely weakened, which was reflected in an HLD-DR value of 27.3% in the admission laboratory in the ICU. Therefore, immunotherapy with immunoglobulin (Pentaglobin) 5 g four times daily was started on the second day of admission. This application was continued for a total of three consecutive days, resulting in a total dose of 60 g administered to achieve adequate immunocompetence.

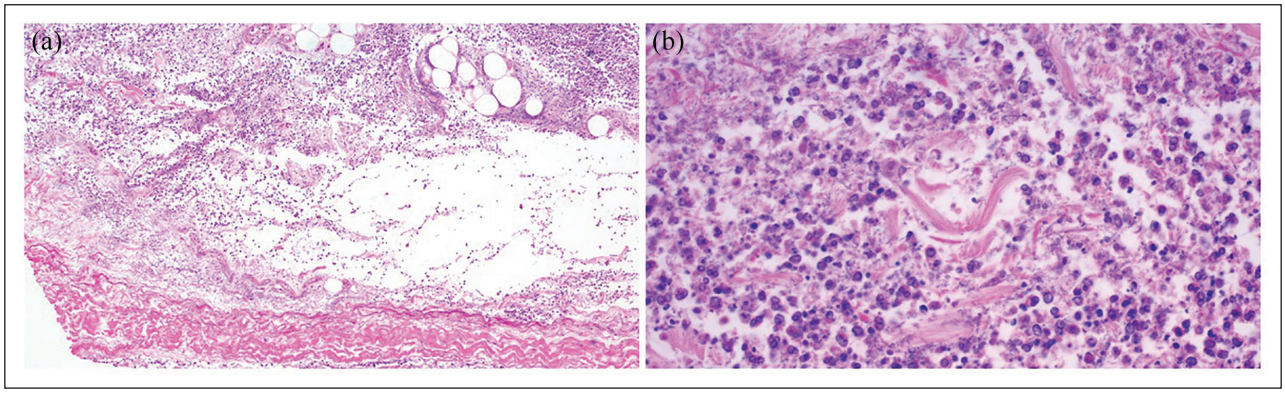

Figure 4. Pathology. (a) Overview of the resection specimen showing extensive necrosis involving the fascia and the perifascial soft tissue (fascia seen as an eosinophilic band at a lower field). (b) Higher magnification shows necrosis and extensive neutrophilic inflammation with entrapped fascia fragments in the midfield.

Further course

After gradual weaning from mechanical ventilation, the patient could be extubated on the seventh day after hospital admission. On the same day, the inflammatory parameters had also decreased almost into the normal range: Temperature, 36.8°C, leukocytes, 15.8×10^9/L; CRP, 694 nmol/l; PCT, 9.51 µg/L; IL-6, 32.5 U/L; LBP, 25.3 U/L; and HLA-DR, 61.2%. Following further stabilisation of the cardiovascular situation, the catecholamines could be continuously reduced and finally discontinued.

Once inflammatory parameters were normalised, the patient could be transferred from the ICU to the normal ward on day 16 after admission. While still in the hospital, a suitable prosthesis for the right thigh was fitted.

Finally, after further recovery, the patient was discharged to rehabilitation on the 26th day after admission to our hospital. The patient was discharged home in good health after a further 3-week stay in a rehabilitation clinic.

Discussion

This case report describes severe necrotising fasciitis caused by STSS in a 54-year-old Caucasian male who was successfully treated surgically and with intensive care by an interdisciplinary clinical team. Early diagnosis and treatment of this syndrome are keys to minimising mortality from this life-threatening condition and reducing the incidence of complications.

It is well known that STSS is a severe, life-threatening infection that can also be caused by GAS. The morbidity and mortality of STSS are mainly influenced by the patient's medical history, that is, existing comorbidities such as diabetes mellitus, peripheral arterial occlusive disease and thus reduced oxygen supply to the tissue, age, site and extent of infection, and delayed in diagnosis and early initiation of therapy.[8] In particular, the combination of a chronic skin lesion in conjunction with long-standing and untreated diabetes mellitus has been identified as an important predisposing factor for invasive *Streptococcus pyogenes* infection in children and adults.[13]

Because STSS can rapidly lead to life-threatening conditions, as mentioned earlier, patients with STSS benefit from very early admission to an appropriate ICU, as was done in this case report. This affects not only adults but also children, and according to preliminary work by Garancini et al., based on data from the WHO, it seems that we are currently facing a new outbreak.[14] This makes it all the more important to deal with this disease and the various treatment options today. Therefore, this work is intended to be a recommendation for action for the therapy of similar cases in order to be able to act rapidly in time-critical situations.

Early debridement and removal of affected tissue up to the point of amputation, as in this case, are important measures that significantly increase the chances of survival.[15]

The primary antibiotic therapy for STSS remains penicillin, to which *Streptococcus pyogenes* is still highly sensitive although penicillin has been widely used in the past.[16] A combination treatment with clindamycin can additionally significantly increase the success of antibiotic therapy.[9] In this case report, the broad-spectrum penicillin piperacillin/tazobactam was started to eradicate as many bacteria as possible. After the bacterium *Streptococcus pyogenes* could be identified in the microbiological culture, the therapy was de-escalated to penicillin G. The antibiotic clindamycin, which was started on admission to the ICU, was added on the one hand because of its additive effect on streptococci and on the other hand because of the possible exclusion of a *Clostridium perfringens* infection.

According to the results of a study by Leijte et al., absolute values of HLA-DR should have no direct correlation to the course of severe sepsis in contrast to several course values.[17] However, after our patient's immediately measured value was extremely low, immunoglobulin therapy was started without delay. We assume that the direct administration of immunoglobulins, as well as the immediate surgical intervention, had a positive effect on the course of our patient's disease.

It is known that acute renal insufficiency associated with STSS is related to a worse prognosis in children.[18] But it also increases mortality in adults. In this case report, we therefore initiated haemodialysis early to preserve renal function in the presence of elevated myoglobin and to reduce mortality. However, it should be considered whether it might have been more appropriate to include a high-capacity filter in the dialysis machine to extract cytokines and other substances before starting immunotherapy. If the immunoglobulins had been administered with the dialysis machine running with a high-capacity filter, they would have been immediately eliminated from the blood and would have had no effect. Given the sepsis associated with the high inflammatory parameters and the weakened immune system, we decided to administer the immunoglobulins immediately. Unfortunately, the HLA-DR was determined only once after administration of the immunoglobulins. However, the result showed a significant increase in immunocompetence. Since the COVID-19 pandemic, there has been increased consideration of whether early haemodialysis is indicated in patients with ARDS,[19] as 'flooding' of the lungs by crystalloids, which are absolutely necessary for the therapy of sepsis, could be avoided. Unfortunately, the results are currently inconclusive, neither in patients with COVID-19 ARDS nor in patients with ARDS – due to another cause.[20,21] However, clinical experience shows that the time for starting dialysis should not be chosen too late.

This case report is presented to illustrate that, on the one hand, rapid initiation of therapy is important in STSS patients and, on the other hand, an interdisciplinary team is needed that can benefit from a large pool of therapeutic options (lung-protective ventilation, dialysis, comprehensive laboratory diagnostics, surgery at any time, microbiological diagnostics, etc.) to successfully manage this disease.

Conclusion

Early diagnosis and treatment of STSS are the keys to minimising morbidity and mortality and thus to successfully treating this still life-threatening disease. It is therefore of immense importance that these patients are treated in a centre that has all the therapeutic options of modern intensive care medicine and an experienced interdisciplinary and interprofessional clinical team.

Acknowledgements

We would like to thank our colleagues from all professional groups in the departments of anaesthesia and surgery at the University Hospital of Erlangen for their work on and with our intensive care patients, which is certainly not always easy.

Contributions

T.S.: Conceptualisation, Project administration, Formal analysis, Investigation, Writing – original draft, Review, Editing.
C.T.: Radiology investigations, Editing.
A.A.: Pathology investigations, Editing.
A.W.: Conceptualisation, Formal analysis, Investigation, Writing, Review, Editing.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: We acknowledge support by Deutsche Forschungsgemeinschaft and Friedrich-Alexander-University of Erlangen-Nurnberg (FAU) within the funding programme Open Access Publishing.

Ethics approval

Our institution does not require ethical approval for reporting individual cases report.

Informed consent

Written informed consent was obtained from the patient for the anonymised information to be published in this article.

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