

Streptococcal Necrotizing Fasciitis with Toxic Shock Syndrome and Rapid Fatal Outcome

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SUMMARY

Introduction Streptococcal necrotizing fasciitis (NF) is a serious soft tissue infection with rapid progression of inflammatory process among superficial or deep fascia, systemic host response to infection leading to toxic shock syndrome (TSS), and multiple organ failure. Lethality is high.

Case Outline A 46-year-old male without co-morbidities was admitted to the Emergency Department with redness, swelling and pain on his right lower leg. He became sick two days earlier with malaise, chills and shivering. On admission he was hypotensive, anuric, with erythematous rash on his face, neck and chest, with acute renal failure and elevated creatine phosphokinase level. During the next several hours, the changes on his right lower leg rapidly spread to the whole leg, followed by skin destruction and subcutaneous bleeding, indicating NF. Aggressive antimicrobial, supportive and symptomatic therapy was initiated immediately and on the same evening surgical intervention was performed. Despite these measures, a rapid development of severe TSS, with lethal outcome, occurred in less than 40 hours after the admission. *Streptococcus pyogenes* (group A β -hemolytic *Streptococcus*) was isolated from the throat, skin and tissue obtained during the surgery.

Conclusion Necrotizing fasciitis is a very serious disease with unpredictable course. For that reason doctors must devote a great deal of attention to early, i.e. timely diagnosis of this disease, whose treatment with a multidisciplinary approach is very important.

Keywords: necrotizing fasciitis; toxic shock syndrome; *Streptococcus pyogenes*

INTRODUCTION

Invasive group A streptococcal (iGAS) infections are a major clinical and public health challenge [1]. They were very frequent in the pre-antibiotic era, but since the introduction of antibiotic therapy their incidence has fallen. However, in the medical literature their reoccurrence has been reported more frequently in the last 10–20 years, particularly among children and previously healthy young persons between 20 and 50 years of age [2]. This is due to the increasing colonization of the general population with invasive strains of group A *Streptococcus* (GAS), a β -hemolytic bacterium [3]. We do not have accurate data on the incidence of iGAS infections in Serbia, while the incidence rate of three cases per 100,000 inhabitants has been reported in some developed countries [4, 5]. About 5–10% of iGAS infections are necrotizing fasciitis (NF) [6]. One of the most severe complications of iGAS infections is streptococcal toxic shock syndrome (STSS). The first cases of STSS were described in 1980, according to the similarities to the clinical syndrome caused by *Staphylococcus aureus* (SA). These include hypotension and two or more signs of renal impairment, coagulopathy, hepatic involvement, adult respiratory distress syndrome, generalized rash, or soft-tissue necrosis [7].

The objective is to present a fulminant form of NF with rapid progression to STSS with fatal outcome.

CASE REPORT

A 46-year-old male patient, plumber by trade, without co-morbidities, was admitted to the Emergency Department of the Military Medical Academy in Belgrade, Serbia, because of inflammatory changes on his right leg, on March 22, 2013. The disease onset was two days earlier with chills and shivering, without fever. On the next day, redness, swelling and pain appeared in his right leg. On admission he was observed by a surgeon, who suspected that it was erysipelas and requested a consultation with an infectious diseases specialist. After a careful examination it became clear that it was a much more serious illness, since local changes were more prominent compared to erysipelas, including epithelial defects and hematoma (Figure 1). The patient was presented with hypotension, initially reversible with saline infusions, tachycardia and renal impairment. For that reason the patient was admitted to the Clinic for Infectious and Tropical Diseases. Objectively, local changes were spreading extensively, suggesting that the disease was developing into a rapidly progressive one (Figure 2). The epithelial defect was more prominent, with worsening hematoma, and the inflammation spread over the entire leg. In the next few hours, hypotension could not be corrected by infusions, renal failure developed, and diffuse, light macular rash appeared on his face, neck and chest. After three hours NF spread to the entire right leg

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Figure 1. Early phase of streptococcal necrotizing fasciitis of the right leg on admission



Figure 2. Streptococcal necrotizing fasciitis of the right leg in the same patient after a few hours

Table 1. Laboratory parameters of the patient with necrotizing fasciitis

Parameter	Date and time of day			
	March 22, 2013 at 12:00	March 22, 2013 at 15:30	March 22, 2013 at 22:00	March 23, 2013 at 06:00
CRP (mg/l)	245	291	/	/
Hemoglobin (g/dl)	141	139	109	107
Leucocytes ($\times 10^9/l$)	5.5	2.87	2.24	3.68
Glucose (mmol/l)	7.2	11.7	5.8	13.3
Creatine kinase (IU/ml)	807	1877	2537	5770
AST (IU/ml)	31	46	52	258
Sodium (mmol/l)	131	/	136	136
Urea (mmol/l)	21.5	27.1	25.9	28.9
Creatinine (mmol/l)	686	705	602	681

CRP – C-reactive protein; AST – aspartate aminotransferase

and hypotension did not respond to inotropic stimulation anymore.

Laboratory parameters of the patient are shown in Table 1.

There was no consolidation of lung parenchyma on his chest X-ray. Abdominal ultrasonography revealed renal parenchyma reduction. There was no gas in the soft tissue, according to the lower leg radiography. Doppler sonography of the leg blood vessels didn't show arterial or deep veins thrombosis. GAS was cultured from pharyngeal and skin swab and from a tissue sample taken during the operation. Antibigram was performed and it showed sensitivity to penicillin, macrolides and clindamycin. Blood culture remained sterile.

Empiric antibiotic therapy with cloxacillin was initiated immediately after the admission. Measures of hemodynamic support were also applied including substitution of water and electrolytes, fresh frozen plasma, albumins and inotropic stimulation with dopamine. Surgical procedure, incision and washing, was performed without fasciectomy, five hours after admission and thereafter the treatment was continued in the intensive care unit with intensive hemodynamic and respiratory support.

Despite all procedures, the course was fulminant with a rapid onset of shock and the lethal outcome in less than 40 hours after the admission.

DISCUSSION

NF is a rapidly progressive soft tissue infection which involves skin, subcutaneous fat tissue, superficial fascia and sometimes deep fascia and muscles [7, 8, 9]. There are two types of NF. Type 1 is caused by polymicrobial flora which consists of one or more anaerobic species and facultatively aerobic bacteria different from GAS and usually affects high-risk patients like elderly, patients with chronic diseases, such as diabetes and alcoholism, immunocompromised patients and patients who have recently undergone surgery. Type 2 is monomicrobial, usually caused by GAS alone, or in a combination with SA, usually affects previously healthy young people and is frequently a rapidly progressive disease [10, 11, 12]. The most severe forms of streptococcal NF are complicated by STSS [8].

In a typical acute presentation the disease begins after an unapparent trauma with rapid development of erythema, swelling and tenderness. In the next few days the local changes evolve to purple bullas and blisters, after which purple lesions become gangrenous. In the next few days those lesions become demarcated with separation of dead skin. In a fulminant course, like in our patient, the development is more progressive with rapid hemodynamic instability, shock and multiple organ failure [9].

European studies showed that patient's age is a very important predictor of lethal outcome of NF. Older patients have the poorest survival rate. Most deaths in younger patients occur in the first two days, as was the case in our patient [4]. According to the Centers for Disease Control and Prevention, case fatality of NF correlates with the seasonal period. Most deaths are registered from December to April [4]. The next very important prognostic factor is the presence of STSS. In patients without STSS mortality is about 30%, while in those with it mortality is about 80–100% [13]. Time of the diagnosis is also a very significant prognostic aspect [14]. Adequate surgical debridement is the next step that determines the outcome of NF, as it was not the case in our patient [15].

Necrotizing fasciitis should be considered when signs of a severe disease are present with even minor skin changes

Table 2. Factors of LRINEC score

Factors of LRINEC score		Points
CRP (mg/l)	<150	0
	≥150	4
Leucocytes (×10 ⁹ /l)	<15	0
	15–25	1
	>25	2
Hemoglobin (g/dl)	>13.5	0
	11–13.5	1
	<11	2
Sodium (mmol/l)	≥135	0
	<135	2
Creatinine (mmol/l)	≤141	0
	>141	2
Glucose (mmol/l)	≤10	0
	>10	1

[16]. In order to make diagnosis as early as possible, in order to distinguish NF from other soft tissue infections, laboratory scoring systems have been developed recently. The most important is the Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score [15, 17]. Basic factors of LRINEC score are presented in Table 2. The LRINEC score greater than or equal to six denotes higher rates of mortality and amputation [18].

In our patient the LRINEC score was eight at admission, suggesting a high-risk patient, even though his local finding was not so prominent. Soon after admission his LRINEC score rose to 10, indicating poor outcome.

Definitive diagnosis is made after sampling tissue taken during the operation and its pathohistological verification. However, that procedure is time consuming and is not useful for the decision on treatment initiation [11].

The treatment of NF must be rapid and requires a multidisciplinary approach. It consists of antibiotics, hemodynamic resuscitation, surgical debridement, intravenous immunoglobulin and hyperbaric oxygenation therapy for

hemodynamic stable patients where it is available [11, 12, 19]. Most studies prefer clindamycin, as in these serious infections bacteria are present in a stationary phase of growth, and in such situations drugs that act as cell wall synthesis inhibitors, which require extensive replication of bacteria, are less effective than drugs that inhibit synthesis of proteins, thus inhibiting synthesis of streptococcal toxins. However, penicillin should be added since some strains of GAS are resistant to clindamycin [20]. Our patient was treated only with cloxacillin because clindamycin was not available at that moment. The decision to choose low spectrum antibiotic was based on the fact that the patient was a young and previously immunocompetent person without co-morbidities, as well as the fact that the course of the disease with TSS indicated type 2 of NF, which is usually caused by GAS alone or in combination with SA. Antibiotic therapy alone is not sufficient because of tissue hypoxia and ischemia that do not permit its adequate delivery to the local tissue [19]. Thus extensive surgical debridement is necessary in order to remove necrotic tissue. Our patient was hemodynamically very unstable, and therefore appropriate surgical intervention was not performed. Incision and washing were done without fasciectomy because of very poor general appearance of the patient. In patients with NF, especially those with STSS, use of high doses of intravenously administered immunoglobulin are much more beneficial than fresh frozen plasma (FFP), as they bind superantigens and enable them to cause strong systemic reaction [12, 21, 22]. Unfortunately, they were not available at the time of treatment, so we used FFP only.

Fatal NF is a possible and not easily predictive disease, which is why a physician must devote a great deal of attention to the early diagnosis and adequate multidisciplinary treatment of it. Sometimes, in the most serious forms, lethal outcome is inevitable even if those measures are achieved.

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Стрептококни некротизирајући фасциитис с токсичним шок-синдромом и брзим смртним исходом

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КРАТАК САДРЖАЈ

Увод Стрептококни некротизирајући фасциитис (НФ) је тешка инфекција меких ткива праћена веома брзом прогресијом запаљења дуж површинских и дубоких фасција и системским одговором домаћина на инфекцију, која може довести до токсичног шок-синдрома (ТШС) и дисфункције органа. Смртност је висока.

Приказ болесника Мушкарац стар 46 година, без коморбидитета, примљен је у Центар хитне помоћи због црвенила, отока и бола у пределу десне потколенице. Разболео се два дана раније, када је осећао малаксалост, језу и дрхтавицу. На пријему је био хипотензиван, ануричан, с еритематозном оспом на лицу, врату и грудном кошу, акутном слабошћу бубрега и високим вредностима креатин-фосфокиназе. У наредним сатима промене су се брзо шириле дуж десне

ноге уз знаке оштећења коже и поткожног крварења, што је указивало на НФ. Одмах је започето агресивно лечење применом антибиотске, супортивне и симптоматске терапије, а исте вечери учињена је и хируршка интервенција. Упркос овим терапијским мерама, дошло је до брзог развоја тешког ТШС и смртног исхода за мање од 40 сати од пријема у болницу. Из бриса ждрела, ране и некротичног ткива узетог током операције изолован је бета хемолитички стрептокок групе А.

Закључак НФ је веома тешка болест непредвидљивог тока. Стога лекар мора да посвети велику пажњу правовременој дијагнози овог обољења, у чијем је лечењу неопходан мултидисциплинарни приступ.

Кључне речи: некротизирајући фасциитис; токсични шок-синдром; *Streptococcus pyogenes*

Примљен • Received: 17/06/2014

Прихваћен • Accepted: 29/09/2014