



Severe form of streptococcal necrotizing fasciitis of the upper limb – diagnostic and therapeutic challenge: A case report

Teška forma streptokoknog nekrotizujućeg fasciitisa ruke – dijagnostički i terapijski izazov

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Abstract

Introduction. Since delay in recognition and effective treatment of necrotizing fasciitis (NF) caused by invasive group A *streptococcus* increases the mortality and disability, the early diagnosis and management of this disease are essential for a better outcome. We presented a patient with a severe form of streptococcal NF of the left upper limb in whom amputation was performed as a life saving procedure.

Case report. A 65-year-old man, previously healthy, suffered an injury to his left hand by sting on a fish bone. Two days after that the patient got fever, redness, swelling and pain in his left hand. Clinical examination of the patient after admission indicated NF that spread quickly to the entire left upper limb, left armpit, and the left side of the chest and abdomen. Despite the use of aggressive antibiotic and surgical therapy severe destruction of the skin and subcutaneous tissues developed with the development of gangrene of the left upper limb. In this situation, the team of specialists decided that the patient must be operated on submitted to amputation of the left arm, at the shoulder. After amputation and aggressive debridement of soft tissue on the left side of the trunk, the patient completely recovered. β -hemolytic streptococcus group A was isolated from the skin and tissue obtained during the surgery. **Conclusion.** In the most severe forms of streptococcal NF of the extremities, adequate multidisciplinary treatment, including limb amputation, can save the life of a patient.

Key words:

fasciitis, necrotizing; streptococcus; arm; amputation; anti-bacterial agents.

Apstrakt

Uvod. S obzirom na to da kašnjenje sa postavljanjem dijagnoze i lečenjem nekrotizujućeg fasciitisa (NF) uzrokovano invazivnim streptokokom grupe A povećava smrtnost i invaliditet, rana dijagnoza i lečenje ove bolesti esencijalni su za bolji ishod. Prikazali smo bolesnika sa teškom formom streptokoknog NF leve ruke kod koga je urađena amputacija, kako bi se spasio život. **Prikaz bolesnika.** Muškarac, star 65 godina i prethodno zdrav, zadobio je povredu leve šake ubodom na riblju kost. Dva dana kasnije on je dobio visoku temperaturu, crvenilo, otok i bol u levoj ruci. Klinički pregled bolesnika nakon prijema ukazao je da se radi o NF koji se brzo širio na celu levu ruku, levu pazušnu jamu i levu stranu trupa. Uprkos agresivnoj primeni antibiotske terapije i hiruškog lečenja, kod bolesnika je došlo do razvoja teške destrukcije kože i potkožnih tkiva sa razvojem gangrene leve ruke. U ovoj situaciji konzilijum specijalista odlučio je da se kod bolesnika mora uraditi amputacija leve ruke u ramenu u cilju spašavanja života. Posle amputacije i debridmana mekih tkiva na levoj strani trupa, kod bolesnika je došlo do potpunog oporavka. Iz kože i mekih tkiva dobijenih tokom operacije izolovan je β hemolitički streptokok grupe A. **Zaključak.** U najtežim formama nekrotizujućeg fasciitisa ekstremiteta, adekvatan multidisciplinarni tretman, uključujući i amputaciju ekstremiteta, može spasiti život obolelog.

Ključne reči:

fasciitis, nekrotizujući; streptococcus; ruka; amputacija; antibiotici.

Introduction

Necrotizing fasciitis (NF) is a severe, life-threatening bacterial infection that causes rapid destruction of skin, subcutaneous tissue, fascia and/or muscle¹⁻⁴. NF caused by invasive group A streptococcus (GAS) may be one of the most dramatic conditions seen in medicine. This type of NF can develop over hours to days usually with a precipitating traumatic event and can deteriorate quickly. The illness is more commonly known as a “flesh-eating disease” that can kill a human in less than a day⁵⁻¹⁰. Since delay in recognition and

subcutaneous tissue, and afterwards partial fasciotomy on the inside of the forearm and upper arm. Despite the applied treatment, the clinical findings and the patient's general condition were getting worse, and the patient was transferred to the Military Medical Academy on December 25, 2013. On admission to the Clinic for Infectious and Tropical Diseases the patient was in poor general condition, tachypneic, with reduced oxygen saturation, hypotensive, tachycardic. The development of severe destruction of the skin and subcutaneous tissues with the development of the gangrene of the left upper limb were present (Figure 1).



Fig. 1 – Streptococcal necrotizing fasciitis of the left upper limb after repeated incisions and partial fasciotomy.

effective treatment increase the mortality and disability, the early diagnosis and management of GAS NF are essential for a better outcome¹⁰⁻¹³. In all patients intravenous antibiotic therapy and aggressive surgical debridement should be urgently initiated. Other modes of surgery, such as amputation, may be required in streptococcal NF of the extremities¹²⁻¹⁷. However, the decision about amputation, although it should save the patient's life, may be difficult and often delayed because of the lack of knowledge of disease nature. Establishing the diagnosis of streptococcal NF can be challenging in treating these patients, and the knowledge of all available tools is the key for the early and accurate diagnosis¹⁸⁻²¹.

We presented a patient with a serious form streptococcal NF of the upper limb and emphasized the importance of the early diagnosis and prompt decision about adequate surgical treatment.

Case report

A 65-year-old man, previously healthy, allergic to penicillin, suffered an injury to his left hand by sting on a fishbone on December 16, 2013. Two days after that he got a very strong pain, redness and swelling of the left forearm and upper arm, followed by chills, and high fever. So, he was urgently admitted to the local hospital. Under the assumption that the patient was a case of cellulitis of the left hand intravenous therapy with amikacin and ciprofloxacin was given. Because the clinical findings of the left hand were worsening, the patient underwent repeated incisions of the skin and

In laboratory findings erythrocyte sedimentation rate was 111mm/1st h, C-reactive protein (CRP) 275 mg/L, erythrocytes $3.09 \times 10^{12}/L$, hemoglobin 95 g/L, leukocytes $20.3 \times 10^9/L$, neutrophils 85%, platelets $146 \times 10^9/L$, glycemia 13.7 mmol/L, sodium 130 mmol/L, potassium 3.1 mg/L, urea 25.5 mmol/L, creatinine 289 umol/L, protein 44 g/L, albumin 17 g/L, with the rapid increase of serum creatine kinase (CK) level to 3090 U/L, and with a slight increase of serum transaminases levels.

Thanks to our past experience, we made the prompt diagnosis of probable streptococcal NF. Right after admission we started with a combined intravenous antibiotic therapy (clindamycin at the dose of 2,400 mg *per* day plus vancomycin at the dose of 2 g *per* day), with the use of fluids, electrolytes, human albumin, fresh frozen plasma, and blood transfusion. At the same time we consulted the team of specialists, and also planned application of emergency hyperbaric oxygenation (HBO). On the second day of hospitalization, a wide incision was made in the area of the left upper limb, with partial excision of necrotic tissue. Clinical examination indicated NF which was instantly and quickly spreading to whole left upper limb, left armpit, and the left side of the chest and abdomen (Figure 2). The patient's Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score^{22, 23} quickly increased to 10, and clearly indicated that it was NF. Culture of smear from the wound and necrotic tissue which were taken during the surgery showed isolated β -hemolytic group A *streptococcus*.



Fig. 2 – Streptococcal necrotizing fasciitis of the left upper limb and chest before amputation of the arm at the shoulder.

Despite the implementation of very aggressive treatment the illness took a very serious course. In this situation, the team of specialists decided that the patient must be submitted to amputation of his left arm, at the shoulder, and on December 28, 2013, shoulder disarticulation was made. In addition, aggressive debridement of soft tissue up to healthy tissue of the left side of the chest was done. After amputation, we continued applying antibiotic therapy and HBO, and the general state of the patient was gradually improving, up to full recovery and the patient was released from the hospital few weeks later.

Discussion

According to the literature streptococcal NF can 'enter' through trauma to the skin, sometimes even minor. Besides others, fish fin injury is one of the predisposing factors for the development of NF, as it happened in the presented patient^{1, 24-26}. The disease can involve any part of the body but primarily the extremities²⁴⁻²⁹. Anaya et al.²⁰ in their study of 150 patients with NF estimated that the extremities were the most common site of infection (in 57.8%) followed by the abdomen and perineum.

Although NF can cause a number of bacterial species, invasive types of GAS are the most important causes of this illness, because the speed at which it can induce local infection, streptococcal toxic shock syndrome (STSS), and death cannot be compared with any other infectious agents. In recent years, hyperacute and subacute variants of NF are increasingly reported in the literature^{6, 24-29}. Mikić et al.⁶ showed a 65-year-old man with STSS, without comorbidities, who died in less than 30 hours after admission, and recently, Kojić et al.³⁰ described a 46-year-old previously healthy patient with fulminant course of NF of the right leg,

who developed rapid STSS and died for less than 40 hours after the first medical examination. In these, as in many other cases, there was no sufficient time to apply appropriate therapy, including the amputation of the limb.

Early diagnosis, and early therapy are the main predictors of NF outcome^{2, 4, 10, 20}. Early diagnosis, extensive debridement and, in extreme cases, willingness to amputate the limbs at a very early stage may be the only intervention that can save the lives of patients. Otherwise, the disease has an almost 100% mortality^{7, 9, 12}. The patient presented in this paper had a subacute form of NF. Therefore, despite the delayed diagnosis of NF, after amputation of his left arm the outcome was favorable. Unfortunately, after the treatment there remained a serious disability. In the literature, there is a consensus that the delay in treatment for more than 6–12 hours or inadequate primary surgical debridement are prerequisites of greater morbidity and mortality, as it happened in the presented patient¹²⁻¹⁷.

The diagnosis of NF and its distinction from the other less fatal soft tissue infections is still notoriously difficult and challenging. The results of a retrospective study have shown that 35% of later NF are misinterpreted like cellulitis or severe non-necrotizing soft-tissue infection, while in another study the authors have found that only 14% of patients with NF are admitted with the right diagnosis. It is essential to accentuate that there are no mandatory "hard signs" for the diagnosis of NF, which leads to the missing early diagnosis in 85% to 100% of all cases¹²⁻¹⁷. This is exactly what happened in the presented patient in whom the initial diagnosis was cellulitis of the left hand.

Necrotizing fasciitis of one or more limbs was a medical emergency which requires prompt recognition and aggressive excision of affected tissues. The diagnosis, however, is a challenge, because the infection is usually confused with a milder condition such as cellulitis. Various tools for reaching an early diagnosis have been suggested but the key is a high level of suspicion³¹⁻³⁴. Reliance upon adjunctive diagnostic tests may delay operative treatment. We believe that the accurate diagnosis of infection can be made clinically and that no investigation can replace meticulous and repeated physical examination. The diagnosis of NF is primarily clinical with corroborating operative findings, so it should be suspected in patients with high fever, symptoms of severe infection and unclear pain of soft tissue. The main sign of the disease is very strong pain.¹ However, thrombosis of the vessels of the skin will lead to necrosis and severe pain will fade as the nerves die, when it comes to the appearance of anesthesia in the most necrotic area³⁵.

Early diagnosis of NF is not always possible due to paucity of cutaneous findings early in the disease therefore high index of suspicion is important in infected cases that are refractory to antibiotics. In the laboratory findings there is elevated number of leukocytes, associated with the increase in CRP, and creatine kinase level. Biopsy of soft tissue and histopathologic verification of NF are useful only in the early stage of disease. Isolation of GAS is most important for making the diagnosis of streptococcal NF^{1, 14, 17, 25}. LRINEC score is a new and very useful diagnostic scoring system for

distinguishing NF from other soft tissue infections. A score greater than 8 is very predictive of NF, which was confirmed by the case of the presented patient^{22, 23}.

The treatment of streptococcal NF may involve an interdisciplinary care team. For example, in the case of the presented patient, the team included the infectious disease specialist, orthopedic surgeons, the vascular surgeon, the plastic surgeon, the anesthesiologist, the radiologist and the microbiologist. Antibiotic therapy alone has been shown to have high mortality rates due to reduced antibiotic delivery in poorly vascularized/necrotic tissue at the infection site. Their application is essential for the full success of therapy. Surgical debridement is required to decrease necrotic tissue load and provide a viable tissue bed amenable to the delivery of antibiotics.^{3, 12-15, 36} Other therapies such as HBO therapy and intravenous immune globulin may be useful as adjunctive treatment in patients with NF but remain controversial³⁷⁻⁴⁰.

Antimicrobial therapy must be directed at pathogens and used in appropriate doses. After having been repeated, operative procedures are no longer needed when a patient demonstrates obvious clinical improvement, and no fever for 48–72 h. NF with or without STSS should be treated with clindamycin and penicillin. Unfortunately, the presented patient was allergic to penicillin. The rationale for clindamycin is based on *in vitro* studies demonstrating both toxin suppression and modulation of cytokine (i.e. TNF) production. On animal studies clindamycin demonstrated superior efficacy to penicillin. Penicillin should be added because of the increasing resistance of GAS to macrolides. Vancomycin, or linezolid should be considered until MRSA infection has been excluded. An acceptable empiric antibiotic regime includes linezolid, which covers MRSA with the additional benefit of inhibiting invasive GAS virulence proteins similar to clindamycin^{3, 12-15, 36}. Taking into account the above mentioned we conducted antibiotic therapy in our patients with clindamycin, and vancomycin since we add suspicion of simultaneous infection with MRSA. The above treatment should be accompanied with supportive measures such as fluid replacement, blood pressure support, analgesia, nutritional support and intensive care involvement etc.

Early and radical surgical excision of necrotic tissue up to healthy tissue for limiting further necrosis of subcutaneous fascia and fat tissue significantly increases survival compared to patients with delayed debridement even for just a few hours^{3, 7, 9, 12-17}, McHenry et al.⁴¹ reported that the average time from admission to operation was 90 hours in non-survivors *versus* 25 hours in survivors. Similar findings were also reported by Wong et al.¹⁶. Angoules et al.¹⁹ reported that patients with NF required an average of 3 surgical debridements, with 22.3% of patients requiring amputation for failure of multiple surgical debridements to control infection. Other authors warn that limb amputation may be necessary to stop the spread of infection in nearly 50% of patients with GAS NF¹⁷⁻²¹. Some of these authors have not found that amputation correlates with survival, but it should be noted, that surgeons are more likely to amputate in more severely

affected cases and therefore skew the mortality rate²¹. Amputation is usually a shorter procedure associated with less blood loss than radical debridement of the skin and fascia and requires less, if any, further reconstructive surgery. Nevertheless, the decision to amputate must be made with great caution in patients with a very proximal involvement, particularly when infection affects the trunk. In these cases, the mutilating procedure may not always control infection nor improve the chances of survival^{17-21, 27}. However, it turned out that in our patient the decision to amputate the arm at the shoulder was correct and timely even though infection had already affected the trunk.

For a long time there were no clear guidelines on limb amputation because of the small number of cases NF. Since 1995, guidelines for undertaking an amputation have been adopted, but they are not a strict protocol²¹. Each team of experts has made the final decision for amputation after discussion between colleagues and the patient in the presence, when possible, of his or her relatives. Tang et al.²¹ suggested some guidelines for decision regarding amputation of a limb with NF. These guidelines include concurrent medical disease with high anesthetic risk (e.g. poorly controlled diabetes mellitus), extensive tissue necrosis with involvement of the underlying muscles, shock requiring more than one ionotropic agent, concurrent vascular insufficiency, rapidly progressing infection with large area of tissue necrosis. In the presented case there was extensive necrosis of the tissues of the left hand with the spread of infection into large areas of the trunk, but the team of specialists was sufficient for the decision on amputation, and that decision proved to be correct.

The worldwide mortality rate of NF reflects the severity of the disease. McHenry et al.⁴¹ summarized the reported mortality rates from different studies. The cumulative mortality rate was 34% (6% to 76%). The mortality was related to age, the percentage of body surface involved, and the presence of hypotension, as well as the time delay between admission to hospital and surgical debridement. Some authors conclude that patients with the involvement of the proximal part of a limb at the time of admission have a high mortality rate, which may imply a longer period from the onset of the disease and therefore an increased delay in adequate treatment start^{2, 4, 7, 9, 10, 25, 26, 28}. The presented 65-year-old patient in whom NF affected the entire left arm and a large part of the left side of the body survived, thanks mainly to adequate treatment.

Conclusion

Necrotizing fasciitis of the limbs caused by invasive group A *streptococcus* is frequently fatal. This is particularly common among patients with the diagnosis established late and late initiated treatment. However, even in the most severe forms of the disease adequate multidisciplinary treatment, including limb amputation can save the life of a patient and reduce the mortality of streptococcal necrotizing fasciitis of the limbs.

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