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Case Report

Necrotizing Fasciitis with Compartment Syndrome of the Lower Leg After Non-venomous Snake Bite in Central Europe: Case Report

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Abstract

Introduction: Necrotizing fasciitis (NF) is a type of necrotizing soft-tissue infection (NSTI) with high mortality rate. Typical clinical status of a patient with NF includes initial symptoms and signs such as non-specific skin changes, fever and localised pain, which later progress to tissue necrosis, sepsis and systemic toxicity. Compartment syndrome can also be a complication of the disease.

Case Presentation: We present a case of 42-year-old Iraqi Kurdish male, who suffered NF after a snake bite in central Europe (the snake was identified as non-venomous; S. pyogenes was isolated from the wound), which later progressed to compartment syndrome of the lower leg. The patient also had positive PCR test for Covid-19 infection at the time of admission. Later, the patient underwent extensive treatment of NF, which included surgical debridement, broad-spectrum antibiotic therapy and intensive support treatment. He survived without significant subsequent impairment.

Conclusion: There are far more clinical cases of secondary infection of the snakebite wound described in tropical climates than continental European climate, in which our case has occurred. Patients with underlying chronic diseases and leucocytosis could be more susceptible to the development of secondary NF with high-grade tissue damage and multi-organ failure. Urgent fasciotomy, optimal antibiotic therapy and intensive care treatment are crucial.

Keywords: Necrotizing Fasciitis; Compartment Syndrome; Snake Bite; *Streptococcus*; Septic Shock

Abbreviations

CK: Creatine Kinase; CRP-C: Reactive Protein; CT: Computed Tomography; MRI: Magnetic Resonance Imaging; NSAID: Nonsteroidal Anti-Inflammatory Drug; NF: Necrotizing Fasciitis; NPWT: Negative Pressure Wound Therapy; NSTI: Necrotizing Soft Tissue Infection

Introduction

Necrotizing fasciitis (NF) is rare, but severe and potentially lethal soft tissue infection, which mostly affects subcutaneous tissue and muscle fascia. It is often described as "flesh-eating", rapidly progressing infectious disease, which can result in sepsis, major necrosis of infected tissue and fatal systemic toxicity if left untreated [1-5]. Although NF can occur at any age, there are some well-known predisposing factors for NF: diabetes and other chronic diseases, malignancies, obesity, kidney and vascular diseases, immunosuppressive therapy, age (above 60 years of age) and the usage of intravenous drugs [1,3]. Early clinical diagnosis, immediate therapy with broad-spectrum antibiotics and aggressive surgical debridement are the three key points in management of NF [1-5].

A pathophysiological process, which leads to NF, usually starts with a skin wound acting as a portal of entry for microorganisms.

After the contamination, bacteria start to proliferate (and release exotoxins), which cause subsequent inflammation and tissue damage. Both infection and inflammation can spread through a large portion of the subcutaneous tissue along the deep fascia (especially in the trunk and limbs, where there are fasciae with greater surface, without any fibrous attachments that would stop the infection from spreading), causing injury and thrombosis of the vessels perforating the fascia, resulting in necrosis of subcutaneous tissue and adjacent skin [1-3].

Patients with NF are usually presented to emergency department with non-specific skin changes, like erythema and skin oedema, which can easily be misidentified as a sign of a milder skin infection, such as cellulitis or erysipelas [1]. Signs and symptoms, which separate patients with NF from patients with other skin infections, are localised, out-of- proportion pain (which can also be absent in patients with diabetic neuropathy, altered mental status, or NSAID therapy; pain can also be wrongly described as post-operative complication), tenderness, fever and hypotension [1,2,4]. Usually, those skin changes quickly develop into more drastic forms, such as bullae with greyish-brown discharge, skin necrosis and tense oedema with underlying crepitus, vesicles and (occasionally) cutaneous anaesthesia [1,4,6]. If NF fully develops, it puts patient's life in danger due to sepsis, multi-organ failure and possible toxic shock syndrome, commonly associated with streptococcal and staphylococcal infections [1-3]. In some circumstances, the infection involves enclosed anatomical compartments, i.e., lower leg compartments. The inflammation (oedema) lifts the pressure inside the affected fascial compartment and compromises the perfusion of it. The process, defined as compartment syndrome, can facilitate further muscle injury and muscle cell death (rhabdomyolysis), which can cause loss of limb and, what is more concerning, life- threatening hyperkalemia, myoglobinuria and kidney failure [7-9].

The fact that it can be difficult to differentiate NF at its initial clinical stages from other, far less devastating skin and soft tissue infections, such as cellulitis, presents one of the main issues in diagnosing NF. When initial skin changes (erythema, soft tissue oedema) progress to more dramatic ones (bullae, "dish-water grey" exudate, skin discoloration and necrosis, tenderness of the affected area with oedema and crepitus), physicians must be aware that there is not much time left to react [1-5]. The progression of the disease is rapid, bullae and blue-grey skin discoloration patches can occur in a period of 24 to 72 hours after onset. In that time, signs of systemic toxicity can also become evident. Fascial and subcutaneous necrosis precedes skin necrosis; muscles can be affected later, when inflammation involves entire fascial envelopes, but not in the initial stages of the disease [2,3].

Clinical findings can be supported with laboratory tests (elevated CRP and CK, leucocytosis, acidosis) and imaging (X-ray, CT, MRI), but the early surgical exploration remains the golden standard for the NF diagnosis confirmation [1-5,8,10]. With exploration, surgeon can determine the extent of infection, assess the need for further debridement (or amputation) and obtain tissue samples for Gram's staining and culture [2].

Treatment consists of surgical procedures, IV antibiotic regime and supportive care in an intensive unit [4,5]. Surgical approach includes removal of necrotic tissue (skin, muscle, bone) in the infected region. As a result, the debridement is usually radical and often mutilating. Patient's wound should be re-explored in 24-48 hours after the initial debridement to assess the further spread of infection (whether the debridement needs to be repeated) and to facilitate wound dressing [4-6].

Until the causative agents are identified, broad- spectrum IV antibiotics for poly-microbial coverage are prescribed. When planning initial therapy, one must include antibiotics to cover potential Clostridium and Streptococcus infections (penicillin), Gram- negative pathogens (piperacillin-tazobactam, cephalosporins, carbapenems) and anaerobes (metronidazole, clindamycin) [4,5,11].

Poly-microbial or type 1 infection is the predominant type (55-75%) of NSTI, commonly found on the trunk or the perineum of an immunocompromised patient. Presentation of NF in the perineum is usually addressed as Fournier's gangrene. Typical for type 1 infection is that there is a mix of aerobic (*Streptococcus* spp., *Staphylococcus* spp., *E. coli*, *Pseudomonas* spp., etc.) and anaerobic (*Bacteroides* spp., *Clostridium* spp.) bacteria isolated [1-5]. There are several predisposing factors for type 1 infection, including diabetic and decubitus ulcers, abdominal, urologic and gynaecologic surgery procedures, and rectal fissures [2]. On the other hand, monomicrobial or type 2 infection can occur in relatively healthy individuals of any age group, usually suffering from soft tissue injury of variable extent. The most common pathogen associated with type 2 infection is group A streptococcus. *S. aureus* is also isolated fre-

quently, but in lesser percentage. The initial soft tissue injury can be of greater extent (crushed limb), but it can also be a minor one (needle puncture wound or a snake bite) [1-5].

In this article, a patient with streptococcal NF is presented. Incidence of streptococcal NSTI ranges from 0,4 to 5 cases per 100.000 people in developed countries. Death rate of these patients is 30-50 % (even up to 80 % by some studies) when treated, but without treatment the infection is lethal [1-4,6,8].

Case Presentation

42-year-old, previously healthy Iraqi Kurdish male, was admitted to the University Medical Center Ljubljana, due to un-identified snakebite and subsequent infection, located on the lower part of his right ankle. Three days after the bite, the patient developed fever with shivering; he also noticed a painful swelling of the right ankle.

The initial physical examination in the emergency room showed fever (40,1°C). At the beginning of the treatment, the patient was hemodynamically stable and his neurological and circulatory status were normal. On the lateral side of the patient's right ankle, two punctiform wounds with swelling and mild redness on the skin could be seen (Figure 1).

Figure 1: Snakebite wound on the right ankle of the patient.

The laboratory results showed leukocytosis (14,1 10^9/L) and slightly elevated CRP (22 mg/L). Hemoglobin levels appeared normal (140 g/L). An X-ray imaging of the patient's right lower limb revealed presence of the gas in the subcutaneous tissue. Due to the COVID-19 pandemic, a nasopharyngeal swab (PCR) test for Covid-19 infection was performed and the result was positive.

An initial empiric wide-spectrum antibiotic therapy with imipenem/cilastatin (500 mg/6h IV) and clindamycin (900 mg/8h IV) was initiated. After the initial treatment, there was a sudden deterioration in the general condition of the patient. Within the next seven hours, he became hypotensive (RR 77/56 mmHg), tachycardic (with a pulse of 110/min) and hypoxic (oxygen saturation of 96%, with the addition of 3 liters of oxygen per nasal catheter). The laboratory findings showed rapid increase of CRP levels (236 mg/L), lactate level (up to 3,13 mmol/l) and procalcitonin level (from 0,17 µg/L to 2.92 µg/L). Pain and the swelling of the right lower leg, ankle and foot were rapidly increasing.

Intensive treatment for septic shock with vasoactive support, corticosteroids and additional fluid infusions was initiated. Due to clinical suspicion of secondary necrotizing fasciitis or compartment syndrome, the patient was urgently operated in general anesthesia. Surgical incision of the skin and the soft tissue with fasciotomy and necrotomy of the right lower leg and foot were performed. Tissue samples were sent for microbiological and histological examination. The sites of surgical incisions were left open, highly absorbable wound dressings were applied (Figure 2).

Figure 2: The affected lower limb before the second surgery. The incisions from the first surgery were left open.

Two days following the first operation, a second radical surgical debridement was performed. The necrotic tissue of the skin, soft tissue and fascia was removed (Figure 3).

Figure 3: Radical surgical debridement with the removal of necrotic soft tissues.

Continuous negative pressure wound therapy (NPWT) of -125 mmHg was applied to the open surgical wound (V.A.C.™, KCI, 3M, San Antonio, Texas, USA) (Figure 4).

Figure 4: Application of NPWT.

NPWT was changed three times, until healthy granulation of the wound bed was achieved (Figure 5). The microbiological results showed presence of *Streptococcus pyogenes*, sensitive to penicillin, vancomycin and clindamycin. No microorganisms were isolated in the blood cultures. Antibiotic therapy was changed to crystal penicillin of five million units/6h IV and was discontinued after two weeks of treatment due to clinical and laboratory improvement.

Figure 5: Granulation of the wound bed.

Histological finding confirmed severe necrotizing inflammation of fat tissue, connective tissue and fascia with presence of coccus bacteria.

On the fifth postoperative day, the fever reappeared (39,0°C), patient coughed and had signs of a cold. The patient was hospitalized at the Clinic for Infectious Diseases and Febrile Conditions, Covid Unit, for supportive treatment of the mild case of Covid-19 infection. After 10 days the general condition of patient was improved, and he was admitted back to Clinical Department for Surgical Infections. Once the treatment with NPWT was completed, the large skin defect was covered using partial thickness skin graft from the thigh (Figure 6).

Figure 6: Coverage of the large skin defect using partial thickness skin graft.

NPWT was applied to the transplant skin area for the duration of 5 days. At the end of the treatment, stable soft tissue coverage was achieved. Patient was discharged from hospital in a good general condition, without local or systemic signs of infection, and with preserved leg and foot function.

Discussion

Our patient was relatively young and in good physical shape. His clinical status at the admission point was close to normal (apart from fever and swelling of his ankle), but it gradually progressed to more serious condition, which was later recognized as necrotizing fasciitis with subsequent compartment syndrome of the right lower leg. The patient also suffered an infection with Sars-Cov-2 virus, which did not significantly affect the outcome of the treatment. Specific clinical features of our patient, like the presence of S. pyogenes inside the wound, patient's age and fitness, and minor portal of microbiological entry (snake bite wound), resemble those specific for type 2 necrotizing fasciitis. However, in our case, one must take in mind the possibility that the tissue injury and the thrombosis of the fascial vessels were (at least partially) caused by thrombogenic and cytotoxic substances in snake's venom, but that is usually a case in tropical environments in Africa, Asia and the Caribbean [6,10-12].

Case reports of secondary infections of snakebites, like our one, have been published in medical literature. However, the frequency of these cases is relatively low; the individual cases are described far more in tropical climates than in non-tropical ones [13,14].

Ballesteros-Betancourt., *et al*. presented the case of a 24-year-old female patient without any relevant associated health condition, who got bitten by *Vipera aspis* snake on the dorsum of her right foot. Initially, there were no significant signs or symptoms of a serious soft tissue pathology, but in the next 48 hours, swelling of the patient's lower right limb (from the groin region to the dorsum of the foot) with associated erythema and intense pain occurred. Pain could be exacerbated with palpation of the swollen region and with passive and active movement of the affected limb. The patient herself was afebrile, hemodynamically stable and neurologically intact. After extensive surgical treatment, the patient was discharged after 30 days. Tissue samples showed macroscopic thrombosis of the supra- and transfascial vessels of the affected tissue, however, no microorganisms were isolated from them. Authors concluded that the cause for the thrombosis were snake's thrombogenic toxins [6].

Hearn., *et al*. reported the case of a 9-year-old Cambodian boy, who was bitten by a cobra on his forearm. Two days after the bite he was admitted to local hospital due to painful swelling of his arm with erythema spreading from his entire arm to his neck and chest. The boy was febrile with tachycardia. After extensive surgical debridement, the examination of the necrotic tissue showed presence of *M. morganii* and *E. faecalis.* Authors' theory was that there were two main factors, that mostly contributed to the development of a secondary infection of the wound, resulting in NF: the extent of necrosis, caused by snake's venom (which acted as an optimal environment for the development of the infection), and the microflora in snake's mouth, which was introduced into the wound during the bite [14].

Kaur and Mahajan published a case report about a 10-year-old girl who was bitten in India. The snake was recognized as Russel's viper (the identification was difficult due to being badly mutilated). At first, the patient was given the anti-snakebite venom and broad-spectrum antibiotics. However, the patient developed subsequent NF with *P. aeruginosa* isolated from the affected tissue. The bacteria were resistant to fluoroquinolones and cephalosporins [13].

Tsai., *et al*. made a study in which medical records of 83 patients with snakebites, admitted to Chia-Yi Chang Gung Memorial Hospital (Taiwan) from June 2010 to July 2016, were reviewed. 16 of them were diagnosed with NF, 25 of them with cellulitis (the latter group did not need any surgical intervention, in contrast to patients with NF diagnosis). The study underlined few risk factors, which could be important for the development of NF from the initial infection of the snakebite wound: leucocytosis (≥ 10000 cells per mm^3), high percentage of segmented white blood cells (over 80%) and the associated chronic diseases, such as hepatitis, cardiovascular diseases, gout, diabetes mellitus and chronic renal failure. The research put an emphasis to prompt surgical intervention in case of developed NF, paired with empirical use of third generation cephalosporins in the antibiotic regime [11].

The similar conclusion as Tsai's was made by Severnys., *et al*. who published a case report about a 42-year-old woman, who was bitten to her right calf by a *Bothrops lanceolatus* snake on the island of Martinique. Tissue necrosis, caused by snake's toxins, facilitated its contamination with *Aeromonas hydrophila* (which was isolated from the blood culture), thus leading to the development of serious soft tissue infection (presumably NF) with large oedema of patient's right lower limb and septic shock. Urgent fasciotomy of

all right leg compartments and anterior compartment of the right thigh with debridement of the necrotic tissue was crucial for patient's survival, according to the authors. After antibiotic treatment and proper dressing of the affected site, the wound healed successfully after 29 days [11,12].

Banda and N'gambi reported another case of post-snakebite NF of the upper limb, but in their case, it progressed even further, to mediastinitis. The patient, an 11-year-old girl from Zambia, was then successfully treated. To authors' knowledge, there was only one other case of NF with mediastinitis reported in medical literature up until their report was published [10].

Secondary infection of the snakebite wound can facilitate the tissue damage, already made by snake's toxins. It can lead to serious soft tissue infection, such as NF with septic shock, which can get even more complicated with the (uncommon) development of compartment syndrome, like in our patient, or even rarer complications (mediastinitis, if the NF affects upper limb) [10,12]. Numerous microorganisms have been found in different species of snakes, from Gram- negative bacteria such as *Morganella morganii*, *Pseudomonas* spp. and *E. coli* (which were usually resistant to many commonly used antibiotics) to Gram- positive bacteria (Staphylococcus spp., *Enterococcus* spp.) and anaerobes (*Bacteroides* spp. and *Clostridium* spp.) [10-14]. In some theory, the venom of certain snakes possesses significant antibacterial properties, which could explain the rarity of secondary infections of the snakebites [14]. Due to these facts, Kaur and Mahajan recommend keeping the patient with the snake bite wound under observation for at least 24-48 hours, regardless of the type of bite [13]. In our case, the snake was not identified.

Conclusion

NF is a life-threatening condition that must be treated surgically to remove necrotic tissue, coupled with application of IV antibiotics. Patients with NF also need supportive care in an intensive unit. Snakebites with secondary infection and possible venom-influenced tissue injury enable the entry point for microorganisms; therefore, these types of wounds should be observed repeatedly. Rapid diagnostics with subsequent surgical treatment are crucial to enable good clinical outcome.

Conflict of Interest

None.

Bibliography

1. Puvanendran R., *et al*. "Necrotizing fasciitis". *Canadian Family Physician* 55.10 (2009): 981-987.

2. Stevens DL and Bryant AE. "Necrotizing Soft-Tissue Infections". *The New England journal of medicine* 377.23 (2017): 2253-2265.

3. Sadasivan J., *et al*. "Necrotizing fasciitis". *Indian Journal of Plastic Surgery: Official Publication of the Association of Plastic Surgeons of India* 46.3 (2013): 472-478.

4. Bonne SL and Kadri SS. "Evaluation and Management of Necrotizing Soft Tissue Infections". *Infectious Disease Clinics of North America* 31.3 (2017): 497-511.

5. Cocanour CS., *et al*. "Management and Novel Adjuncts of Necrotizing Soft Tissue Infections". *Surgical Infections* 18.3 (2017): 250-272.

6. Ballesteros-Betancourt JR., *et al*. "A non-infectious necrotizing fasciitis of the lower limb after a snakebite: Case report and literature review". *Injury Extra* 44 (2013): 6-8.

7. Guo J., *et al*. "Acute compartment syndrome: Cause, diagnosis, and new viewpoint". *Medicine* 98.27 (2019): e16260.

8. Reichert JC., *et al*. "Necrotizing streptococcal myositis of the upper extremity: a case report". *BMC Research Notes* 10.1 (2017): 407.

9. Long B., *et al*. "Evaluation and Management of Acute Compartment Syndrome in the Emergency Department". *The Journal of Emergency Medicine* 56.4 (2019): 386-397.

10. Banda CH and N'gambi C. "Necrotizing fasciitis with mediastinitis following snakebite envenomation". *SAGE Open Medical Case Reports* 7 (2019): 2050313X18823090.

11. Tsai YH., *et al*. "Necrotizing fasciitis following venomous snakebites in a tertiary hospital of southwest Taiwan". *International Journal of Infectious Diseases: IJID: Official Publication of the International Society for Infectious Diseases* 63 (2017): 30-36.

12. Severyns M., *et al*. "Case Report: *Bothrops lanceolatus* Snakebite Surgical Management-Relevance of Fasciotomy". *The American Journal of Tropical Medicine and Hygiene* 99.5 (2018): 1350-1353.

13. Kaur H and Mahajan G. "An interesting case of snake bite with necrotizing fasciitis". *Journal of Pediatric Critical Care* 5.3 (2018): 91.

14. Hearn P., *et al*. "Necrotizing fasciitis complicating snakebite in Cambodia". *ID Cases* 2.3 (2015): 86-87.