CASE REPORT

Soft tissue injury of the lower extremity complicated by type II necrotising fasciitis highlighting the need for astute clinical practices and proper treatment

Alexander Sabre,¹ Carlos G Robles,¹ Patricia Krisar-White,² Laurie Farrielli³

¹Universidad Autonoma De Guadalajara Medical School, Guadalajara, Mexico

²University of Medicine and Pharmacy Iuliu, Cluj-Napoca, Romania

³Department of Internal Medicine, Scottsdale Healthcare Shea Medical Center, Scottsdale, Arizona, USA

Correspondence to

Alexander Sabre,
alexandermsabre@gmail.com

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SUMMARY

Necrotising fasciitis (NF) is a soft tissue bacterial-derived infection characterised clinically by fulminant tissue destruction of the poorly blood-supplied muscle fascia and overlying subcutaneous fat. Although these infections first appear as minor superficial manifestations, they are capricious in nature and often lead to sepsis, organ failure and high mortality. We report a case of type II necrotising fasciitis in a 39-year-old Caucasian female patient who presented to the emergency department with cellulitis of her right foot and lower leg that rapidly developed into tissue necrosis. The patient course is of unique interest due to progressive history over a 104 days time frame with complications following surgical treatments and outpatient follow-up. We highlight the importance of early detection and pertinent clinical awareness from a wide range of medical specialties that were involved in this case, and how this process is critical, in order to properly diagnose and treat NF-derived tissue infections.

BACKGROUND

To our knowledge there is no literature elaborating on the fulminant course of necrotising fasciitis (NF) following multiple failed repairs involving inpatient and outpatient setting over an extended period of time. Approach considerations to this case were extensive and based on all relevant patient information. The patient's history of traumatic injury involving a body of water included differential causative bacteria such as *Aeromonas species*, *Edwardsiella tarda*, *Erysipelothrix rhusiopathiae*, *Vibrio vulnificus* and *Mycobacterium marinum* referred commonly in the literature as the acronym AEEVM.¹ Early on in patient course, positive anti-streptolysin O titres quickly ruled out these organisms as a potential cause of infection. In this case, due to high precision medical cooperation and suspicion among many specialties including internal medicine, general surgery and infectious disease, diagnosis of type II NF was based on considering the following: obesity as a predisposing factor; history of recent traumatic injury to the extremity affected; progressive tissue destruction based on clinical appearance within 24 h period; ASO titre positive, ruling out type I NF; and surgical involvement finalising diagnosis with tissue pathology. This patient course over a total period of 104 days, from initial inpatient presentation to final outpatient follow-up, highlighted how problematic NF type II infections are in dictating and following treatment

course. Doctor and patient goals of treatment in this case were directed to ensure full limb recovery and to not consider radical measures unless all other options were exhausted and the situation turned dire. Serendipitously, even after all the complications of drug interactions, failed flap procedures and extensive tissue destruction, the patient was able to make a complete recovery. Final patient follow-up was only significant for minor scar tissue impeding movement of the ankle that was planned for outpatient care from a physical therapist.

The goal of our article was to present a clinical case of type II NF and its extended progression, give detailed background information on what constitutes these infections including presentation, virulence factors and above all else to provide clinicians important information on how to properly recognise, diagnose and treat type II NF soft tissue infections. Owing to the progressive disposition of these infections and because of the significant mortality associated with type II NF varying between 14% and 34% of reported cases, it is important to take approaches with highly keen clinical practices in order to prevent the high mortality which is a hallmark of NF even when plans follow optimum therapy regimens.

CASE PRESENTATION

A 39-year-old obese Caucasian woman presented to the emergency department of our hospital with fever, chills, sweats, fatigue, appetite change, nausea, myalgia, a rash and pain localised to the dorsum of her right foot that was described as red, warm to the touch, tight and swollen and also included an area of a scabbed wound between the second and third toes. On detailed history the patient informed us that 2 weeks prior to admission she acquired a small open wound where the scab was located due to an injury sustained from a tile in a public swimming pool. The patient also admitted to picking at the wound with her fingers, as it was irritating. Medical history was significant for depression and Osgood-Schlatter disease; surgical history included two caesarean sections, lap band surgery and bilateral inguinal hernia repair. Family history was significant for diabetes, atrial fibrillation and hypertension with her father, and a sister with kidney failure. All else was unremarkable. The patient denied use of tobacco, alcohol or recreational drugs. Current medications included wellbutrin and paroxetine. Her allergies at time of admission included only demerol.

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On admission, vital signs were a blood pressure (BP) of 135/86 mm Hg, heart rate (HR) 135/min, temperature 38.1°C respiratory rate of 16/min. Physical examination revealed fever, tachycardia, clear lung sounds, no organomegaly and a hot oedematous brawny rash over the dorsum of her foot, covering the first, second and third toes, with a concurrent lesion on her medial right calf of 42.7 mm in diameter (figure 1). Laboratory values showed a haemoglobin of 11 g/dL, haematocrit of 34.8%, mean corpuscular volume (MCV) 74.1 fL, white cell count (WCC) of $6.6 \times 10^3/\text{mL}$, neutrophil 83.1%, basic metabolic panel (BMP) revealed sodium 137 mmol, potassium 3.5 mmol, chloride 101 mmol, creatinine 0.9 mg/dL and blood urea nitrogen (BUN) 10 mg/dL. Of note, ASO titres taken were positive with a value of 260 units. Intravenous cefazolin was started and the patient was placed on telemetry inpatient. At this time, surgery and infectious disease was consulted.

Approximately 24 h after admission, despite the course of treatment of antibiotics, the patient was found to be spiking fevers as high as 39.3°C; she experienced a rapid increase and spread in erythema; right lower extremity swelling with developing blisters and necrosis over the greater toe area raised concern for early type II NF based on positive ASO titres and suspected group A streptococcus (GAS)-derived cellulitis. MRI was ordered, and surgical consult was initiated with the patient undergoing fasciotomy of the wound. The patient antibiotic regimen added intravenous cefepime and intravenous clindamycin and continued the intravenous cefazolin. On the third inpatient day drawn blood cultures from admit and tissue cultures from surgery failed to grow a microorganism. On inpatient day 4, the patient developed a haematoma on the right foot and was taken back to the OR for debridement and clean-up of the wound area.

On inpatient day 5, intravenous antibiotics were switched to a peripherally inserted central catheter (PICC), along with a free flap reconstruction of the areas that underwent debridement using skin autograft from the lower flank and upper thigh. At this time blood cultures failed to find a causative organism and tissue cultures were negative.

On inpatient day 7 the patient developed a haematoma of the autograft that required drainage. At this time the patient was moved from telemetry to intensive care unit since symptoms of fever and erythema of the skin did not improve and WCC became elevated, along with the dropping of haemoglobin and

haematocrit (H&H) to 6.1 g/dL and 19.5%, respectively. The debridement procedure along with drop in H&H was extensive and required blood transfusions.

On inpatient day 8 another debridement and removal of the non-viable flap was performed. The patient also developed an extensive erythrodermal rash all over her body that was suspected to be hypersensitivity either from an undiagnosed latex examination glove allergy or to the antibiotic regimen. As a result of this precipitous change in patient course, only intravenous penicillin G was given.

On inpatient day 9 the WCC count suddenly spiked to $37.9 \times 10^3/\text{mL}$ warranting investigation for cause, with differential including possible occult fungal infection, early systemic inflammatory response syndrome (SIRS), early sepsis, failed flap or a possible urinary tract infection. This was all superimposed by the severe drug reaction that was likely due to the intravenous cefepime. As a result of these complications in patient treatment, the antibiotic regimen was changed to intravenous tygacil, intravenous micafungin and oral ciprofloxacin. These changes were necessary to the regimen and were evident on inpatient day 10 as the rash improved significantly. Repeat cultures returned, showing no growth in urine or blood. From inpatient day 11 onwards the WCC count continued to decrease and the patient was considered medically stable for discharge on inpatient day 13. Outpatient treatments consisted of continuous wound care, intravenous tygacil every 12 h and oral lactobacillus.

TREATMENT

Laboratory techniques are only complementary in the diagnosis of NF. Blood cultures are problematic as there is not high sensitivity; true positive cultures are only found in 60% of type II infections versus 20% in type I.² Imaging techniques such as X-rays, Doppler ultrasound, CT or MRI studies help show gas in tissues as well, and can be used to delineate how far the infection has spread into soft tissues, but cannot be used for pure diagnostic measures. Other laboratory mechanisms of clinical relevance in NF infections are CBC showing elevated WCC, chemistry panel with a decreased BUN, decreased serum sodium levels and markedly elevated creatine kinase.

NF is considered a surgical emergency and remains the gold standard in care; it is the only effective manner of establishing diagnosis and effective treatment. Diagnosis is via explorative visualisation with tissue biopsy and culture for definitive measurement. Pathology of samples generally presents with acute tissue destruction, thrombosis of vessels and massive inflammatory process in fascia lines.³ Surgical treatment consists of aggressive debridement of all necrotic tissue and surrounding affected tissues, concurrent re-evaluation in 24 h, and continued debridement if considered necessary. This time-based aggressive stance towards patient care has the best outcome as noted in the literature; greater than 24 h intervention is a factor for increased mortality.²

The use of negative-pressure wound therapy (NPWT) to assist in wound healing is routine in management of soft tissue injury and applied to a wide range of clinical situations such as surgical debridement of acute or chronic wounds and reconstruct surgery.⁴ Advantages of this assisted device compared to conventional moist saline dressings was found in the literature to better immobilise graft ensuring less chance of shearing, and to make quantitative improvements of skin graft success by reducing the number of repeat grafts and decreasing hospitalisation time.⁵

Exudates from infection site or biopsied tissue help provide clinicians to determine what organism(s) are the cause of infection. Antibiotic regimens are only used to prevent secondary

Figure 1 Initial patient physical presentation. Note the erythematous rash covering the dorsum of the foot including covering the first, second and third toes.

effects of localised infection; general approach considerations are based on using broad spectrum therapy; these include cases of absent microorganism growth on culture medium or inadequate time elapse. In-depth dosage and plans are beyond the scope of this discussion in therapy; we will highlight the empirical recommendations from the current literature by regimen and by specific classes. Options for clinicians to consider as management are the usage as follows⁶:

- ▶ Usage of carbapenem or β -lactam/ β -lactamase inhibitor with clindamycin; or
- ▶ Amingoglycoside or fluoroquinolone, plus metronidazole;
- ▶ Owing to high prevalence of hospital-acquired infections and their prevention, the addition of anti-methicillin-resistant strains; vancomycin, daptomycin or linezolid.

OUTCOME AND FOLLOW-UP

Outpatient day 14–59 after discharge from hospital the patient's condition was stable and she continued outpatient treatments under the same regimen. The wounds on her calf and foot were still open and carefully dressed and kept clean to prevent concurrent infection.

On day 60 the patient was readmitted to hospital for a new skin graft procedure over the dorsum of the right foot. Physical examination showed exposed tendons with thick purulent drainage (figure 2). Laboratory values were WCC $5.9 \times 10^3/\text{mL}$, red blood cell $3.85 \times 10^3/\text{mL}$, haemoglobin of 8.9 g/dL, haematocrit of 28.6%, platelets of $323 \times 10^3/\text{mL}$, lymphocyte 27.9%, BUN 5 mg/dL. The patient underwent surgery for right lower extremity wound consisting of debridement of scar tissue and skin autograft from the right upper thigh, plus the placement of a wound vacuum-assisted closure (VAC) device (figure 11). The current medications at this time of hospitalisation were cefazolin, wellbutrin, colace, lactobacillus, multivitamin and paroxetine. On day 61, the patient autograft was successful, the VAC device was removed and the patient was discharged.

On final day 70, the patient was seen in outpatient setting for follow-up. At this time, the calf was well healed but the foot had healed with extensive scarring over the dorsal surface. Physical examination of the wound showed serous drainage on the dorsum of the foot and pink granulation tissue. The patient presented with decreased range of motion (ROM) of the ankle in her daily activities. The end plan of care for her was to involve physical therapy to help increase ROM in the right

ankle. Final correspondence occurred on patient day 104 with patient symptoms only of slight swelling of foot, the grafted tissue at this time was completely resolved (figure 3).

DISCUSSION

NF infections are composed of two distinct bacterial aetiologies: type I polymicrobial infection origin which is beyond the scope of this report, or type II GAS based.² Important virulence factors are present in GAS that characterise infection, spreading to deep fascia tissue planes through venous and lymphatic channels. Stevens *et al* described the changing potential of GAS from rheumatic fever to toxic shock-like syndrome concluding with the importance of 'scarlatina toxin'. Renamed the M antigen, this filamentous cell membrane protein acts as a super antigen in vivo on macrophages and possesses antiphagocytic qualities; cases of streptococcal toxic-shock syndrome that have this factor have been associated with 50% increased incidence of NF.³ Other important factors take precedence in type II NF infection over those previously discussed. GAS possess vimentin, a bacterial-derived cell component that the literature hypothesises may help the organism localise to the exact site of muscle injury due to increased surface expression of microtubules. This theorem elucidates the clinical course of NF type II: infection spreads to deep fascia and travels along planes through venous and lymphatic channels.⁶ This pathway of destruction starts with the deeper tissues, and then spreads to the muscle fascia and overlying subcutaneous fat due to poor blood supply. Muscle tissue is relatively spared destruction until late in the disease process. The course of infection involving only deep tissue early in the disease process and with overlying tissue appearing unaffected until advanced in course make these infections onerous. If clinical symptoms have not alerted suspicion, patients often progress to septicemia, developing shock and multiorgan failure. Cytokine upregulation as mentioned earlier with M antigen-derived propagation of MHC II macrophage receptors is believed to contribute to these clinical findings of shock and massive tissue destruction which characterises NF infection.⁷

Epidemiology

There is an incidence of 3.5 cases of GAS infections per 100 000 individuals in USA, with NF infections making up approximately 6% of these cases.⁸ Significant mortality is associated with NF by both subtypes, 21% with type I and 14–34% with type II.⁹

Figure 2 Inpatient day 60: readmission for secondary graft attempt. Photo details a prepped wound for the skin autograph of the dorsum of right foot and greater toe. Thick discharge is noted in wound area.

Figure 3 Final outpatient follow-up day 104. Image shows extensively scarred granulation tissue covering the dorsal surface of right foot and greater toe.

Necrotising soft tissue infections are associated with predisposed conditions such as non-steroidal anti-inflammatory drug (NSAID) use, recent surgery, immunosuppression, traumatic wounds and obesity, with diabetes being a particularly important risk factor.¹⁰ Important clinical manifestations of NF include fever, soft tissue involvement with pain out of proportion with visual findings, rapid progression to swelling, brawny oedema, dark red induration and bullae, and end with presentation of necrotic skin. Laboratory work-up frequently includes elevated WCCs and creatine kinase levels with decreased BUN and sodium.² Reliance on blood culture is precarious, as it is positive in only 60% of cases with GAS.⁸ Imaging studies include MRI, CT and Doppler of soft tissues in order to delineate infection progression. Following clinical suspicion of NF it is imperative for clinicians to understand current treatments based on the literature. This condition is considered a surgical emergency and a greater than 24 h delay in surgery was a factor for increased mortality.² NF can only be diagnosed with explorative surgery of affected areas and treatment consists of early aggressive surgical debridement of tissue necrosis along with empirical antibiotic therapy in order to control the spread of infection. Following surgical course, open wounds involving soft tissue require special techniques to ensure proper healing process, with NPWT offering many clinical advantages compared with traditional care. NPWT versus control in clinical trial of soft tissue was associated with significant reduction in loss of graft areas (zero vs 4.5 cm) and median duration of hospitalisation (13.5 vs 17 days).¹¹

Predisposing factors of infection are centralised around comorbid conditions that are catalysts for a wide range of disease processes that are systemic in nature; these conditions are immunosuppression, obesity and diabetes. Diabetes, as the literature suggests, is a particularly important pre-existing condition that NF infection occurs with more frequently. Reasons for this increased susceptibility are outside the scope of our discussion, but clinicians should be aware that NF infections will not only occur with greater propensity in this population, but will affect in greater instances the head, neck and perineum as well.¹⁰ An interesting predisposing condition is the possibility between NSAIDs and development of type II NF infections. Although the exact mechanism of action is not fully elucidated, the proposed association is believed to be attributable to the inhibition of neutrophil function and the alteration of cytokine release. It may also be secondary to the use of NSAIDs in their functional purpose of analgesia and antipyrogen, and may mask signs of inflammation, delaying diagnosis and allowing for further progression.² The final kind of predisposing factor of significance is traumatic injury that is unsterile in its origin, posing a risk for infection with NF. Although certainly a rare cause of NF, traumatic unsterile injury is a real possibility in development of disease, as demonstrated by our case presentation.

Learning points

- ▶ It is important to consider necrotising fasciitis (NF) infection as differential in a setting of: FOA, sepsis, pain in soft tissues out of proportion with physical findings, crepitus over tissues and increased creatine kinase levels.
- ▶ NF diagnosis is established surgically via visualisation; and tissue biopsy with associated culture of site for definitive measures.
- ▶ Surgical debridement is the only treatment and consists of multiple removals and empirical antibiotics to help prevent sepsis and secondary effects of infection.
- ▶ NF infections follow a clinical course that even with proper treatment often have systemic effects, end organ destruction and high mortality.
- ▶ Early treatment <24 h of progression has best mortality outcomes, therefore it is imperative for clinicians to be knowledgeable in recognition of NF and to begin prompt treatment.

Competing interests None.

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