Necrotizing fasciitis – two case reports and literature review

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ABSTRACT: Introduction: Necrotizing fasciitis (NF) is a rare, rapidly progressing infection of the skin and subcutaneous tissue. NF can lead to massive tissue necrosis, resulting in sepsis, septic shock and death. In this disease, it is important to quickly diagnose and implement appropriate treatment.

Aim: Analysis of the diagnostic and therapeutic process in two clinical cases and a review of the literature on the methods of diagnosis and treatment of necrotizing fasciitis.

Material and methods: The medical data of two patients hospitalized in the St Alexander Hospital in Kielce from December 2022 to June 2023 due to necrotizing fasciitis were analyzed. Also literature search across PubMed, Medline and Research Gate databases from 2000 up to 2023 was performed. We reviewed English literature according to Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines. The following keywords were used: necrotizing fasciitis, etiopathogenesis, pathophysiology, management.

Results: The research group consisted of two male patients with NF after trauma, in different parts of the body. Based on the clinical examination, the results of laboratory and imaging tests, a diagnosis was made and appropriate treatment was initiated. Despite the applied treatment, one patient died as a result of progressive multiple organ failure.

Conclusions: Despite advances in diagnosis and treatment, including universal access to antibiotics, necrotizing fasciitis still cause high mortality. The microbiological complexity of the majority of cases and non-specific symptoms make the diagnostic and therapeutic process difficult. Taking into account necrotizing fasciitis each time in the differential diagnosis of inflammation of the skin and subcutaneous tissue, especially based on trauma, will allow to reduce morbidity and mortality in this disease.

KEYWORDS: debridement, management, necrotizing fasciitis

ABBREVIATIONS
CRP – C-reactive protein
CT – computed tomography
ED – emergency department
ICU – Intensive Care Unit
LRINEC – Laboratory Risk Indicator for Necrotizing Fasciitis
MRI – magnetic resonance imaging
NF – necrotizing fasciitis
NSAID – non-steroidal anti-inflammatory drugs
PEG – percutaneous endoscopic gastrostomy
PRISMA – Preferred Reporting Items For Systematic Reviews And Meta-Analyses

INTRODUCTION
Necrotizing fasciitis (NF) is a rare, rapidly progressive infection of the skin and subcutaneous tissue [1]. It affects superficial and deep fascia and, in some cases, also muscles [2]. Most commonly, the involved tissues are those within the perineal and extremity areas, with the head and neck region being affected less frequently [1]. The disease can quickly lead to massive tissue necrosis resulting in sepsis, septic shock, and death [3]. Therefore, prompt diagnosis and implementation of appropriate treatment are of great importance in this disease entity.

NF is most prevalent in males over the age of 50 [2]. According to the literature, factors increasing the risk of necrotizing fasciitis include immunosuppression, type 2 diabetes, alcoholism, or obesity [2, 3]. Necrotizing fasciitis begins with slight redness or swelling accompanied by pruritus and fever in the area of the wound, usually of traumatic origin [1]. Then, symptoms escalate rapidly, the increased swelling may be accompanied by severe pain, and necrotic lesions appear on the skin [4]. Patients may also experience weakness or nausea [4]. NF requires immediate treatment, with early and radical surgical excision of all lesions and broad-spectrum antibiotic therapy being the treatment of choice [5–7].

Despite the advances in diagnostic and therapeutic methods, the diagnosis of necrotizing fasciitis is often belated, resulting in high mortality rates [8, 9]. Herein, we are presenting a description of two clinical cases along with a review of the available literature on the methods for diagnosis and treatment of NF.

MATERIAL AND METHODS
We analyzed the medical records of two patients hospitalized for necrotizing fasciitis at the St. Alexander Hospital in Kielce between December 2022 and June 2023. Data from medical history and clinical examination, as well as laboratory results, including microbiological cultures, were analyzed. We retrospectively assessed...
original articles, meta-analyses, and clinical case reports related to necrotizing fasciitis, with terms necrotizing fasciitis, etiopathogenesis, pathophysiology, and management being used as keywords. Duplicate papers and cases were removed after being imported into the bibliography management software.

RESULTS

Patient 1.

A 56-year-old male patient had presented to the ED due to a deteriorating condition of a local wound inflicted by a concrete slab falling onto his leg three days before. The patient had also reported fever of up to 39°C. The patient had no history of chronic treatment while abusing alcohol. During hospitalization within the ED, the patient was diagnosed with hitherto untreated hyperthyroidism and atrial fibrillation. Since the injury, the patient had been using topical NSAID ointments and had not used antiseptics when changing the dressings on the right lower leg wound.

Physical examination upon admission revealed tachycardia and fever of above 38°C. Attention was drawn to maceration and desquamation of epidermis of the right shank and thigh with accompanying blisters and necrotic lesions (Fig. 1.).

Laboratory analyses revealed elevated levels of C-reactive protein (545 mg/L), D-dimers (1364 ng/mL), creatinine (1.7 mg/dL, eGFR = 44.50 mL/min/1.73m²), and creatine kinase (337 U/L) as well as hyponatremia (132 mmol/L). No other abnormalities were found in laboratory tests. Upon retrospective assessment using the LRINEC scale, the score of 7 was assigned.

X-ray of the right lower leg revealed an area within the proximal third of the tibial shaft potentially corresponding to periosteal reaction and post-traumatic lesions. For this reason, the patient was consulted by an orthopedist who excluded muscular injury and crural fracture. Diagnostic examinations were extended to include soft tissue ultrasound scanning which revealed a massive swelling of the soft tissues within the lower leg extending to the distal third of the thigh. At the lower leg level, the image was blurred by the swelling which suggested the presence of intramuscular and perimuscular fluid. Following the initial diagnosis, the patient was admitted to the Department of General Surgery.

Upon admission, wound and blood cultures were taken for screening for aerobic and anaerobic bacterial infections. In addition, broad-spectrum empirical antibiotic therapy consisting of piperacillin with tazobactam and clindamycin was implemented. Over the first few days, the treatment was mainly conservative, with dressings being changed with the use of antiseptics, and limited debridement being performed. Due to rapidly progressive necrosis of the skin and subcutaneous tissue of the right leg, the patient was qualified for radical surgical debridement on the 3rd day of hospitalization (Fig. 2.).

The cultures showed abundant growth of Streptococcus pyogenes and Stenotrophomonas maltophilia. Targeted antibiotic therapy was implemented on the basis of the antibiogram, including vancomycin, meropenem, and sulfamethoxazole trimethoprim. Multiple debridements in the operating theater setting were required throughout the hospitalization period. In addition, negative
Pressure therapy as applied in cycles of 5–6 days was included in the management regimen, with wound debridement being performed upon dressing changes. The treatment resulted in an improvement of the general condition, a decrease in inflammatory parameters, and regression of edematous lesions as confirmed by a control ultrasound of soft tissues.

On the 38th day of hospitalization, after a negative result of screening for Streptococcus pyogenes had been obtained from the wound, the patient was transferred to the Burn Treatment Centre in Siemianowice Śląskie for reconstructive procedures. The local condition at the time of the transfer is shown in Fig. 3.

**Patient 2.**

A 72-year-old male patient had been admitted to the ED due to increased swelling of facial soft tissues accompanied by dyspnea and fever of over 39°C. The patient reported having experienced an injury within the upper lip area four days prior to presentation. He had used topical NSAID ointments, no antiseptics. The patient presented with a history of type 2 diabetes, hypertension, nicotinism, and alcoholism.

Upon admission, the patient was in grave condition, drowsy, complying with simple commands. Physical examination revealed hypotension, tachycardia, bilateral dry rales over the lung fields, and fever of 39.3°C. In addition, necrosis of the upper lip area with associated bruising was noted upon physical examination (Fig. 4.).

Laboratory investigations revealed elevated levels of CRP (414.1 mg/L), procalcitonin (34.31 ng/mL), D-dimers (2743 ng/mL), and creatinine (2.55 mg/dL, eGFR = 24.1 ml/min/1.73m²) as well as hyponatremia (132 mmol/L). Upon retrospective assessment using the LRINEC scale, the score of 9 was assigned.

During his hospitalization within the ED, the patient was subjected to a computed tomography (CT) scan of the head and craniofacial area in which massive soft tissue edema of the head and neck region was visualized (Fig. 5.). The patient was admitted to the Department of Anesthesiology and Intensive Care due to the features of multiple organ failure in the course of septic shock. At the Department, the patient was intubated and ventilator therapy was implemented in a lung-protective regimen due to increasing respiratory failure. In addition, microbiological culture samples were taken from the blood and the wound. Antiedemic therapy, fluid therapy, sedation, pressor amines and broad-spectrum antibiotic therapy with meropenem, clindamycin, vancomycin, and fluconazole were implemented.

Blood and wound cultures revealed the growth of S. pyogenes. Targeted antibiotic therapy was implemented on the basis of the antibiogram, including piperacillin and tazobactam as well as continuation of clindamycin. As a result of the treatment, a decrease in inflammatory parameters was achieved.

During patient’s hospitalization within the ICU, an attempt at awakening and extubation was made, albeit no verbal-logical contact could be established. Due to the abnormalities observed in neurological examination after extubation, a CT scan of the head was acquired to reveal no palpable pathologies. The patient was consulted surgically several times throughout his hospitalization – due to the location of the lesions, significant coagulation disorders, and thrombocytopenia, limited mechanical debridement of the upper lip area was performed and accompanied by enzymatic debridement. Regression of the necrotic tissue area was achieved as a result.
NF is a rare disease [6]. Its prevalence in men is ten times higher than in women [1], with the overall incidence of between 0.3 and 15 cases per 100,000 individuals [7]. Due to the diagnostic difficulties and the lack of specific symptoms, the incidence is considered to be underestimated [3, 11]. Late diagnosis results in the spread of necrotic lesions and worsens the prognosis [12, 13]. The most common symptoms as reported by patients include local tenderness or pruritus, redness of the skin, and fever [1]. The skin covering the lesions, initially unchanged, becomes warm, erythematous, and tender after a few days [5]. Typically, tissue necrosis develops on days 3–5 after the onset of the disease [5].

NF is a rapidly progressive disease with a high mortality rate [6]. Depending on the literature, the mortality rates range from 20% to 35% [1, 11, 14]. The infection can be the result of a minor wound or scratch [14], as in the two cases described herein. NF results in extensive, rapidly progressive necrosis involving the skin, subcutaneous tissue, and fascia [6]. The necrosis is caused by microemboli within the vasculature of the affected tissues [5]. Necrotizing fasciitis is usually observed within the lower extremities and anogenital region while being less common within the soft tissues of the upper extremities or the head and neck region [1, 14].

There are known risk factors contributing to the development of necrotizing fasciitis as well as worsening the prognosis. According to Misiakos et al., these factors include uncontrolled type 2 diabetes, atherosclerosis, alcoholism, obesity, immunosuppression, use of non-steroidal anti-inflammatory drugs, and congenital and acquired immune deficiencies [3]. In addition, the aforementioned factors increase the risk of the disease progressing with associated sepsis and septic shock [3]. Both patients presented herein as case studies had belonged to the aforementioned risk group. In addition, in both of these cases, necrotizing fasciitis was accompanied by sepsis.

Microbiologically, two types of necrotizing fasciitis can be distinguished. The more common NF of type I consists in an infection with mixed bacterial flora [5] whereas the less common NF of type II consists in an infection with a single bacterial species [5]. Regardless of the type of necrotizing fasciitis, the most common causative agent is Streptococcus pyogenes [4]. Bacterial flora involved in type I NF may consist of Gram-positive bacteria such as Staphylococcus aureus, Streptococcus pyogenes, and Enterococci, Gram-negative aerobic bacteria such as Escherichia coli and Pseudomonas spp, and anaerobic bacteria such as Bacteroides and Clostridium [6]. In type II NF, the infection is usually caused by gram-positive cocci such as Staphylococcus aureus and Streptococcus. In the presented cases, type I NF was identified in Patient 1 while type II NF was identified in Patient 2.

In Patient 1, the infection was due to Streptococcus pyogenes and Stenotrophomonas maltophilia, whereas in Patient 2, Streptococcus pyogenes was the only etiological agent.

NF is usually caused by gram-positive cocci such as Staphylococcus aureus, Enterococci, Gram-negative aerobic bacteria such as Escherichia coli and Pseudomonas spp, and anaerobic bacteria such as Bacteroides and Clostridium [6]. In type II NF, the infection is usually caused by gram-positive cocci such as Staphylococcus aureus and Streptococcus. In the presented cases, type I NF was identified in Patient 1 while type II NF was identified in Patient 2.

Due to the nonspecific and sparse symptoms, the diagnosis of necrotizing fasciitis is extremely difficult in the first few days after the penetration of the infectious agent [5, 7]. According to the available literature, an accurate diagnosis of NF can be established in only 1/3 of cases [8, 9, 15]. The pain in necrotizing fasciitis is disproportionate to the area of injury [6]. In the course of the disease, a piercing pain within the affected area may last for the first few days, particularly in trauma patients, suggesting a tear or complete rupture of the muscle [5], as was the case of Patient 1 who had been initially diagnosed with damage to the gastrocnemius muscle of the calf. However, it should be kept in mind that necrotizing fasciitis is more common in individuals with type 2 diabetes, who present with impaired perception of pain due to diabetic neuropathy [1, 16]. In addition, with extensive necrosis, pain receptors are damaged; as a result, pain experienced by patients with advanced necrotic lesions in NF may be of trace intensity [4].

Over the first few days of the disease, symptoms in the form of pain, redness, and warmth of the skin, as well as fever may not be intense, causing delays in patients' reporting at the physician's and hence in accurate diagnosis [13]. Along with the course of the disease, blisters may develop in addition to erythematous skin lesions [1]. In the case of infection with anaerobic bacteria, subcutaneous crepitus may be noted on physical examination [6]. In Patient 1 described herein, physical examination revealed maceration and epidermal desquamation of the lower leg and right thigh, along with necrotic lesions. Patient 2, on the other hand, presented with swelling of the facial soft tissues with necrosis and bruising of the upper lip.

The extensive use of antipyretic and anti-inflammatory drugs distorts the clinical presentation and hinders diagnosis. Notably, both patients described herein had used NSAID ointments, the use of which constitutes a risk factor for necrotizing fasciitis [5]. The patients had also not used any antiseptics for traumatic wound care.

The differential diagnostics of skin and subcutaneous tissue inflammations, including necrotizing fasciitis regardless of its microbial type, is difficult due to the similarities in clinical presentation [7, 17]. Unfortunately, no NF-specific laboratory assays are available [18]. Standard investigations include blood counts with smear, coagulation panel, and the serum lactate, creatine kinase, and C-reactive protein levels [6]. Some patients with necrotizing fasciitis also present with elevated aminotransferases [7]. Confirmation of the agent responsible for NF is based on the cultures taken from the affected tissues or from blood in the case of generalized infections [6]. One should keep in mind that cultures should be taken from tissues located as deep as possible, since material collected from superficial tissues may be not sufficient for identification of the causative agent [17]. Proper collection procedure is important as targeted antibiotic therapy is subsequently implemented in patients on the basis of antibiograms established from the culture results [17].

Due to the difficulties associated with the diagnosis of necrotizing fasciitis, Wong et al. had developed the LRINEC scale, with leukocyte, hemoglobin, sodium, glucose, creatinine, and C-reactive protein values being taken into account to screen for possible NF cases [10]. A LRINEC score of above 6 is indicative of a high risk
of necrotizing fasciitis [10]. As shown by meta-analyses of research data, the LRINEC scale can be applied in detecting NF while having no predictive value in assessing prognosis [19, 20]. As shown by Fernando et al., a low LRINEC score does not rule out necrotizing fasciitis due to the low sensitivity of the indicator [21]. The LRINEC score should always be related to the clinical presentation and physical examination findings [21]. In the cases described herein, the LRINEC scores were evaluated retrospectively, with the scores of 7 and 9 being ascribed to Patients 1 and 2, respectively).

The low sensitivity of the LRINEC scale prompted Wu et al. to develop a modification of the tool (m-LRINEC scale) [22]. In the modified scale, the CRP assay was replaced by hs-CRP assay (high sensitivity), and diabetes as well as chronic kidney disease was added to the scale as NF risk factors [22]. Within the m-LRINEC scale, necrotizing fasciitis is indicated by the score of 17 or higher [22]. According to the authors, the m-LRINEC scale is characterized by higher sensitivity and specificity rates as compared to the classic scale [22], although this claim needs to be analyzed in multicenter studies. Due to the broader inaccessibility of hs-CRP determinations, it is difficult to use the m-LRINEC scale in the Polish condition. Therefore, the m-LRINEC scale was not used for the assessment of the risk of necrotizing fasciitis in the cases described herein.

Classic imaging diagnostic methods, such as X-ray, are not applicable in the diagnostics of necrotizing fasciitis [6]. Magnetic resonance imaging (MRI) is the modality of choice in assessing the extent of soft tissue infection [5]. MRI combined with physical examination facilitates the assessment of the extent of potential necrotic tissue debridement [23]. However, access to MRI is limited in the acute surgical settings [16]. The more widely available CT scanners can also be applied in the diagnosis of necrotizing fasciitis [16]. According to Salati et al, CT scans present with 100% sensitivity and 80–98% specificity in relation to the detection of NF [5]. Both MRI and CT scans reveal edema spreading along the fascia [17]. However, it is important to note that within the first few days of necrotizing fasciitis, subcutaneous edema is usually not visualized in imaging studies [17]. Ultrasound scans are also used for diagnostic imaging of necrotizing fasciitis [5]. In addition to subcutaneous edema, findings include fluid collections and abscesses; however, the presentation is not NF-specific [24]. In Patient 1, an X-ray of the right lower limb revealed an area within the proximal third of the tibial shaft, possibly corresponding to periosteal reaction and post-traumatic changes. In this case, diagnostic examinations were expanded to include soft tissue ultrasound which revealed massive swelling of the soft tissues within the lower leg extending to the distal 1/3 of the thigh. In Patient 2, on the other hand, a CT scan of the head and craniofacial area revealed massive soft tissue edema within the head and neck region. One should remember that diagnostic imaging must not delay surgical management, which is the mainstay of treatment of necrotizing fasciitis [17, 23].

Surgical elaboration to remove necrotic tissues should be performed as quickly as possible [5]. Debridement reduces the extent of necrotic lesions and decreases the risk of tissue loss and amputation, leading to reduced mortality [25]. Surgical debridement is the gold standard in the treatment of necrotizing fasciitis [5, 6]. It should be as extensive as possible so as to remove all necrotic tissue. Patients may require multiple debridements during hospitalization for the affected areas to be prepared for reconstructive procedures such as skin grafting, as in the case of patient 1 described herein. Patients with NF within the extremities may require amputations aimed at limiting the source of infection [6]. The problem with necrotizing fasciitis within the head and neck region consists in the specific nature of the area [26]. Surgical debridement in the facial region should be as extensive as possible, yet limited [26]. In the described case of Patient 2, enzymatic debridement was used in addition to surgical debridement due to significant thrombocytopenia and coagulation disorders that resulted from septic shock.

In addition to surgical management, broad-spectrum empirical antibiotic therapy covering potential etiological agents is the second essential element in the treatment of patients with necrotizing fasciitis [6, 7]. No Polish guidelines are currently available with regard to antibiotic therapy in NF. According to the guidelines of the Infectious Disease Society of America, vancomycin or linezolid in combination with piperacillin and tazobactam, with carbapenems or with ceftiraxone and metronidazole should be used in first-line antibiotic therapy when NF is suspected [7, 17]. Clindamycin should also be included in therapy when necrotizing fasciitis is suspected to be due to *Staphylococcus aureus* or *Streptococcus pyogenes* infection [17]. Empirical antibiotic therapy should then be modified in a targeted manner based on the results of swab cultures and antibiograms derived therefrom [6]. In the case of Patient 1, piperacillin with tazobactam and clindamycin were used in the first-line treatment. Patient 2, on the other hand, received a combination of meropenem, clindamycin, vancomycin and fluconazole. In both cases, empirical antibiotic therapy was replaced by targeted antibiotic therapy after the antibiogram results were obtained.

In addition, patients with necrotizing fasciitis are treated with analgesics, aggressive fluid therapy, and vasoconstrictive drugs for septic shock [6]. It should be kept in mind that any patient with suspected necrotizing fasciitis being due to the most common etiological agent, *Streptococcus pyogenes*, should be subjected to empirical isolation lasting a minimum of 24 hours from the start of antibiotic therapy [27].

**CONCLUSIONS**

Despite the advances in diagnosis and treatment, including widespread access to antibiotics, necrotizing fasciitis is still associated with a high mortality rate. The microbiological complexity of most infections and non-specific symptoms make the diagnostic and therapeutic process difficult. Inclusion of necrotizing fasciitis in the differential diagnostic algorithms as followed in all cases of dermatitis and subcutaneous tissue inflammation, especially those on traumatic background, should reduce the morbidity and mortality rates associated with the disease while education of patients on the proper management of traumatic wounds is necessary to reduce its incidence.

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