Research Article **AJODRR (2021) 4:45**

American Journal of Dermatological Research and Reviews
(ISSN:2638-1893)

Necrotizing fasciitis at the extremities and its management

Hatim ABID[1*], Mohammed EL IDRISSI[1], Abdelhalim EL IBRAHIMI[1], Abdelmajid ELMRINI[1], Nissrine AMRAOUI[2], Sara ELLOUDI[2], Hanane BAYBAY[2], Fatima Zahra Mernissi[2]

[1]Department of osteoarticular surgery B4, HASSAN II teaching hospital, Fes, Morocco.
[2]Department of dermatology HASSAN II teaching hospital, Fes, Morocco.

ABSTRACT

We report in the light of a literature review the results of 28 patients treated for Necrotizing Fasciitis (NF) at the extremities between 2012 and 2017 with a view to a prospective study with longer following up and a greater number of patients.

Keywords: Necrotizing Fasciitis; extremities; treatement

***Correspondence to Author:**
Hatim abid
Imm 87, appt 4, rue Sidney, hay ouafae 2, narjiss, Fes; Morocco.

How to cite this article:
Hatim ABID, Mohammed EL IDRISSI, Abdelhalim EL IBRAHIMI , Abdelmajid ELMRINI,Nissrine AMRAOUI, Sara ELLOUDI, Hanane BAYBAY, Fatima Zahra Mernissi. Necrotizing fasciitis at the extremities and its management.American Journal of Dermatological Research and Reviews, 2021; 4:45.

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Website: https://escipub.com/

Introduction:

The term of necrotizing fasciitis (NF) was created by Wilson in 1952 [1] for a rare infection characterized by a rapidly progressive inflammation and fatal infection of the fascia and subcutaneous tissue with secondary necrosis of involved tissues [2]. It may start at the skin and subcutaneous tissues to define cellulitis [3,4,5]. It mostly spreads by lymphatic and blood route [3,6]. When muscles are also involved then it may be termed as necrotizing myositis [5]. Despite improved diagnostic tools and management of treatment in recent years, NF still has a high mortality rate ranging from 6% to 76% [2]. The causative bacteria may be aerobic anaerobic or mixed that get access in from traumatic skin or mucus barrier [7]. Several predisposing factors have been identified in the literature as diabetes mellitus, immune compromised state, vascular insufficiency, cancer, alcoholism, chronic liver, chronic renal [8,9,10,11]. It may occur as a complication of several medical intevention such as cardiac catheterization, sclerotherapy, diagnostic laparoscopy [6,11] or bone plate removal [12]. It is more common in underdeveloped countries than developing countries, more common in adult age than paediatric and more seen in men than women [13,14,15].

Patients and methods:

We retrospectively reviewed all necrotizing fasciitis cases, Treating from January 1, 2012 to December 31, 2017. Demographic data, clinical features, site of infection, type of comorbidities, microbiological and laboratory findings and outcomes were analyzed. Diagnosis was made first by operation and based on the presence of necrotic fascia and purulent discharge with a foul fish-water odor, and secondairy on histopathological findings of surgical specimens showed neutrophils and bacterial clumps infiltration between collagen bundles with focal necrosis. The study population was 28 patients. The area of involvement was calculated using the modified burns assessment criteria of Lund and Browder [16]. Only patients with NF confined to the extremities lower were included in the study excluding patients with NF of other areas.

Results:

In all, there were 28 patients, 19 male and 9 female, 22 survived (80%) and 6 died (20%). The age distribution varied from 38 to 64 years of age with the greatest number of patients being in the 41 to 50 years class interval. (Table 1). The most common comorbidity were diabetes mellitus in 12 patients (43%), renal failure in 6 patients (21.5%) and peripheral arterial disease in 4 patients (14%). Six patients had no comorbidity (Table 2).

Table 1: Age distribution

Age distribution (n=28)				
Age	Surviving group (n=22)		Non-surviving group (n=6)	
	Male	Female	Male	Female
0-10	0	0	0	0
10-20	0	0	0	0
20-30	0	0	0	0
30-40	2	2	0	1
40-50	9	3	3	1
50-60	4	2	1	0
60-70	0	0	0	0
Total	15 (68%)	7 (32%)	4 (67%)	2 (33%)

Table 2: factors associated with NF

Factor	Number (%)	Survived (n=22)	Died (n=6)
Diabetes	12 (43%)	10 (45%)	2 (33%)
Renal failure	6 (22%)	3 (14%)	3 (50%)
Peripheral arterial disease	4 (15%)	3 (14%)	1 (17%)
No comorbidity	6 (20%)	6 (27%)	0

Local erythema, fever and pain were the most common clinical features at presentation in 25 (90%), 22 (78%) and 18 (64%), respectively. The infection involved the upper limb in 4 cases (14%) (Figure 1 and 2), the lower limb in 24 cases (86%) and bilateral lower limb in four cases (14%). Area of involvement was on average 11% in the survivors compared to 10% in those who died. A single organism was identified in 14 patients (50%) and multiple pathogens were isolated in 6 patients (20%) and no organism was identified in 8 patients (30%). The most common Gram positive bacteria were group A Streptococcus, followed by methicillin-resistant Staphylococcus aureus (MRSA) and methicillin-sensitive Staphylococcus aureus (MSSA). Escherichia coli was the most common Gram negative bacteria isolated in 8 patients (Table 3).

Figure 1: Preoperative view of a necrotising fasciitis of the upper limb

Figure 2: Intraoperative view of surgical debridement of necrotising fasciitis extended to the anterior compartment muscles of the forearm

Table 3: Bacteriological profile

Germs	Distribution (%)
Group A Streptococcus	48%
Staphylococcus aureus	44%
Escherichia coli	38%
No organism identified	28%

Discussion:

The annual incidence of NF is estimated at 500 to 1000 cases with a prevalence of 0.40 cases per 100000 population [17]. It is seen to have a predilection for men and affects all age groups, particularly middle-aged and elderly patients [18]. In the review of the literature, the median mortality ratio ranges from 8.7 to 76% [19]. Without treatment, the mortality rate approaches 100%. Anaya et al [20,21] have demonstrated that infection of the lower extremities is the most common site of NF, followed by the abdomen and the perineum. NF of the upper limbs is rare [20,21,22]. In our series, the sex ratio male/female was 2.11. The age distribution varied from 38 to 64 years of age and the greatest number of patients were between the 41 to 50 years class interval. The infection involved the upper limb in 4 cases (14%) and the lower limb in 24 cases (86%) where it was bilateral in four cases (14%).

NF can be classified based on anatomy and in this context its named Fournier's gangrene when it occurs at the level of the perineum and the scrotum. NF can also be classified according to depth of infection in which we distinguish necrotizing adipositis which is most common, necrotizing fasciitis and necrotizing myositis.

Concerning microbial source of infection, NF is called type 1 when it is polymicrobial and which represents approximately 55% to 75% of all NF, type 2 for monomicrobial infection caused by group A Streptococcus either alone or in association with Staphylococcus aureus and type 3 commonly found in coastal communities, when necrotizing infection is caused by Vibrio vulnificu by exposition to warm sea water, although this is not universally agreed on and finally type 4 caused by fungal infections found mainly in the immunocompromised host [3,20,21,23,24,25,26,27,28,29,30,31,32]. In our

context, a single organism was identified in 14 patients (50%), a multiple pathogens were isolated in 6 patients (20%) and no organism was identified in 8 patients (30%). The most common Gram positive bacteria was group A Streptococcus and Escherichia coli was the most common Gram negative bacteria isolated in our series.

It is generally agreed that microbial invasion of the subcutaneous (SC) tissues occurs either through external trauma or direct spread from a perforated viscus or urogenital organ. Bacteria produce endo and exotoxins that cause tissue ischemia, liquefactive necrosis, and often systemic illness. The extension of the infection and necrosis is facilitated by the synergistic action of the virulence factors of bacteria and the specific factors of the host of which the most frequent are diabetes mellitus, liver cirrhosis, chronic heart failure, obesity, alcohol abuse, immunodeficiency, systemic lupus erythematosus, Addison's disease, pre-existing hypertension, and peripheral vascular disease. Infection can spread as fast as 1 inch per hour leading to skin necrosis at a later stage [19,33,34,35,36,37,38,39,40]. In our series, the most common comorbidity were diabetes mellitus which was present in 12 patients (43%), renal failure noted in 6 patients (21.5%) and peripheral arterial disease found in 4 patients (14%). Six patients had no comorbidity and external trauma was the main etiology.

Patients with NF usually present with the classic clinical triad of symptoms : local pain, swelling, and erythema. In addition vital sign abnormalities such as tachycardia (>100 beats/min), fever, hypotension (SAP < 100 mmHg) and tachypnea (>20/min) and loco-regional symptoms like skin necrosis and hemorrhagic bullae are observed in advanced forms and allow to guide the diagnosis of the NF [41,42]. In our context, local erythema, fever and pain were the most common clinical features at presentation in 25 patients (90%), 22 (78%) and 18 (64%) respectively.

Laboratory results in this disease are not usually specific. However, certain laboratory findings can help the clinician to differentiate NF from other skin diseases specifically white blood cell count, C-reactive protein, hemoglobin, Na, serum creatinine and serum glucose which are elevated. Several laboratory-based scoring systems have been proposed for establishing early diagnosis of NF [43,44]. The Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) proposed by Wong et al is one such example (Table 4) [45,46]. A score of less than or equal to 5 meant a probability of less than 50% for developing NF. A score of 6–7 meant 50%–75% risk of NF whereas any score more than 8 is a high indicator to more than75% risk of NF [47].

Table 4: Laboratory Risk Indicator For Necrotising Fasciitis score [45]

Variables	Value	LRINEC score point
C-reactive protein (mg/L)	< 150	0
	>150	4
White blood cell (cells/mm3)	$<15*10^3$	0
	$15-25*10^3$	1
	$>25*10^3$	2
Hemoglobin (g/dL)	>13.5	0
	11.0-13.5	1
	<11.0	2
Sodium (mmol/L)	>135	0
	<135	2
Creatinine (mg/dL)	<1.6	0
	>1.6	2
Glucose (mg/dL)	<180	0
	>180	1
Score ≥ 8 : High risk for NF (>75%) Score = 6-7 : Intermediate risk for NF (50%-75%) Score ≤ 5 : Low risk for NF (<50%)		

Table 5: Modified Laboratory Risk Indicator for Necrotising Fasciitis score [46]

Parameters	Range	Score
Laboratory		
C-reactive protein	>150mg/dL	4
Total white cell count	<15*10⁶/mm3	0
	15-25*10⁶//mm3	1
	>25*10⁶//mm3	2
Erythrocyte count	<4*10⁶/µl	1
Haemoglobin	>13.5g/dL	0
	11-13.5g/dL	1
	<11g/dL	2
Creatinine	<135mmol/L	2
Fibrinogen levels	>750mg/dL	2
Clinical		
Pain	Mild/None	0
	Intermediate	1
	Strong	2
Fever	≤37.5˚C	0
	37.6-37.9°C	1
	≥38°C	2
Tachycardia	>100 beats/minute	1
Signs of acute renal injury	No	0
	Yes	1
Score ≥ 8 : strong suspicion for NF Score = 6-7 : suspicion for NF Score < 6 : No suspicion		

The combination of the score with clinical findings (fever, tachycardia, renal failure and complained about strong/very strong pain) (Table 5) espacially in the case of mmuno- compromised patient increase significantly the positive predictive value of the score to 93% [48,49,50]. In our practice we adopt this attitude which allows us to optimize our diagnostic and therapeutic decision.

Imaging investigation can help to establish the diagnosis of NF. Plain x-ray which can show gas formation in the soft tissue has low sensitivity and specificity. Computed tomography (CT) and magnetic resonance imaging (MRI) are more sensitive and specific than plain x-ray as to the highlighting of the extent of tissue infection, fascial swelling, inflammation and gas formation with better accuracy provided by MRI for which we report a sensitivity of 90% to 100% and specificity of 50% to 85% for detecting NF [51,52,53,54]. In our context, we systematically performed standard X-rays in all our patients and more rarely the CT scan in order to specify the extent of the infection, especially near the roots of the limbs and vasculo-nervous pedicles.

The gold standard modality for diagnosis of NF remains operative exploration during which we objective typically necrotizing infection and intraoperative biopsy will show in early disease stage superficial epidermal hyaline necrosis, dermal edema, and polymorphonuclear infiltration into the dermis. In late stages, all tissue

layers and subcutaneous (SC) ducts demonstrate variable levels of necrosis [55,56]. Successful treatment of NF requires the com- bination of surgical debridement, antibiotics, hyperbaric oxygen therapy (HBO) and Intravenous Immunoglobulin (IVIg) therapy.

Concerning surgical debridement, the literature considers it as the the cornerstone of therapy [40]. In this context numerous studies have shown that the most important determinant of mortality is timing and adequacy of initial debridement. The relative risk of death related to inadequate initial debridement was 7.5 times greater and it was 9 times greater when the procedure was delayed 24 hours from the time of initial hospitalisation [25,56]. Surgical management is indicated for patients displaying intense pain, skin color change, skin ischemia with blisters and bullae, altered mental status, hypotension and metabolic acidosis [3,57]. Incisions should be performed parallel to Langer's lines to achieve better surgical wound healing and less scarring [3,58]. Boundaries of the excision should be comprised of healthy and bleeding tissue and an average of three debridements, spaced 12 to 36 hours apart, are needed to obtain control of severe infection [25,59,60]. Amputation must be considered with the extent of infection to joint or most muscle groups involving the recovery of an useless extremity after the debridement and also when the infection is rapidly spreading toward the torso [21,24]. Wound management after debridement should be left open and treated with wet-to-dry dressings initially. Once the infection is controlled, Vacuum-assisted closure dressings are recommended to enhance granulation, reduce wound surface area and decrease the time required for wound care approximately fourfold [61,62]. For patients with extensive loss of muscle or exposed bone and with whom the wound does not needed additional debridement, full-thickness skin graft (Figure 3), split-thickness skin graft (Figure 4) free or rotational flaps are necessary for proper coverage [40].

Figure 3: Intraoperative view of a full thikness skin graft recovery after toes amputation, debridement and wound granulation

Figure 4: Split-thickness skin graft in the thight after debridement and wound granulation
a) Intraoperative view b) Postoperative view on the fifth day c) Postoperative view in the second month

Concerning antibiotic therapy, it is recommended today in initial antibiotic regimen for empiric coverage, taking into account the resistance of microbes and the relative decrease in the incidence of clostridial infection, to prescribe vancomycin, linezolid, daptomycin, or quinupristin/dalfopristin [28,29]. In addition, clindamycin and quinolones remain a useful agents which offer excellent soft-tissue penetration and can be used to cover anaerobic organisms, group A streptococcus and gram-negative organisms [40]. Antibiotics should be administered for up to 5 days after local signs and symptoms have resolved for a mean duration of 4–6 weeks [63]. In our daily practice, we attach great importance to aggressive early surgical debridement to optimize the chances of salvaging affected limbs and improve the survival of patients in the case of severe forms in addition to appropriate antibiotic coverage and support of systemic effects of necrotizing fasciitis until the formation of granulating tissue at the wound, to perform at this stage the close/cover procedures of the soft-tissu defect.

The use of intravenous immunoglobulin (IVIg) therapy remain controversial as to their efficacy [64,65]. This agent seems to be able to bind bacterial exotoxin, and therefore limiting the systemic cytokine surge associated with systemic inflammatory response syndrome [66,67]. If used, IVIg should be restricted to severe forms with in the case of staphylococcal or streptococcal NF [68,69].

The use of hyperbaric oxygen therapy (HBO) in NF which is based on animal and human studies shows that hyperbaric conditions inhibit infection and exotoxin elaboration especially in the case of anaerobic bacteria [70,71,72]. Clinical studies have yielded conflicting results concerning morbidity and mortality benefit related on the use of HBO for NF [73,74,75]. For this, meta-analysis are necessary to resolve these contradictory findings in order to establish clear recommendations on the use of HBO as treatment of NF.

Looking at studies for the past ten years, the mortality rate of NF varie between 6% and 33% [24,76,77,78]. Nawijn et al [79] reported in their systematic review and meta-analysis an average mortality rates with extremity necrotizing fasciitis around 20% over the past 20 years. In upper extremity preexisting comorbidities and patients presenting with septic symptoms had a greater risk of dying [80,81]. Indeed, a higher ASA classification and base deficit at admission have been linked to higher mortality [82]. In lower limb, the factors associated with increased risk of postoperative mortality are age >60 years, PTT >38 seconds, serum albumin <2.0 mg/dL, coagulopathy, ASA class IV-V, COPD, postoperative ARDS, and postoperative septic shock [83]. In addition, the time to surgery influences the outcomes. In this context, early surgical treatment of NF within 12 hours is essential for reducing the mortality rate [79]. In our series, we report 22 survivors and 6 deaths, which gives us a mortality rate of around 21%.

Concerning the risk of amputation, it ranges from 6% to 28% while the amputation rate of studies assessing the upper extremity varies between 6% and 36% [22,60,84,85,86,87]. Increased risk of amputation was associated with age >52 years, male gender, serum sodium <133 mEq/L, serum creatinine >1.2 mg/dL, internationa normalized ratio >1.4, hematocrit <33%, diabetes mellitus and sepsis [83]. Patients not succumbing to NF have very high morbidity and require a prolonged recovery period. About that, Elliot and colleagues [60] found 82% morbidity in a review of 198 patients. Noted complications included nosocomial infection (76%), ventilator-dependent respiratory failure and adult respiratory distress syndrome (29%), acute renal failure (32%), seizure (5%), stroke (4%), cardiac arrest (3%), and heart failure (2%).

Conclusion:

Early clinical suspicion and adequate surgery are key to improving survival of patients with NF. A multiparametric approach incorporating various clinical and laboratory parameters seems necessary to optimize the management of this fatal pathology.

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