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Case Report

Necrotizing fasciitis caused by mono-bacterial gram-negative infection with *E. coli* – the deadliest of them all: A case series and review of the literature ☆

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ABSTRACT

Introduction: Unlike other skin and soft tissue infections, necrotizing fasciitis (NF) is a very rare but potentially fatal condition. Common organisms causing NF are poly-microbial (type I) infection with mixed organisms and mono-bacterial gram-positive infection with mainly streptococci (type II). Mono-bacterial gram-negative NF is a rare form of NF that is not included in the current classification.

Case series: We report four cases of mono-bacterial gram-negative NF caused by *E. coli*. All patients presented in septic shock and showed landscape-like skin necrosis and pain out of proportion. Radical debridement and escalation of antibiotic treatment was performed in all patients. Short-term survival was 50%. Two patients died of multiorgan failure. Two patients survived short term: One patient was amputated through the knee but died six months later of metastatic prostate cancer. One patient was covered with

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split thickness skin grafts and died three months later of catheter-associated sepsis with endocarditis.

Discussion: Recent findings suggest adding a type III fasciitis, which is caused by mono-bacterial gram-negative organisms. As patients are getting older with even more comorbidities, mono-bacterial gram-negative NF will be an increasing problem for physicians treating soft tissue and skin infections.

In oncologic diseases, liver cirrhosis, renal diseases or otherwise immunocompromised patients, mono-bacterial gram-negative NF with *E. coli* is underestimated. Therefore, in these patients, antibiotic treatment should cover Gram-negative organisms including *E. coli*. However even with adjusted antibiotic treatment and radical debridement, the short-term survival and long-term outcome are poor.

Introduction

Necrotizing fasciitis (NF) is a rare form of skin and soft tissue infections with high mortality caused by infection with liquefactive necrosis that spreads along the deep fascial planes. The hypercoagulable state leads to thrombosis of perforating vessels and necrosis of the skin. Clinical features usually consist of pain out of proportion, local swelling, erythema, warm skin, bullous lesions, skin necrosis, crepitus, and septic shock. Diagnosis is made by clinical and intraoperative findings and can be confirmed by histological and microbiological specimens. Key feature to diagnosis is pain out of proportion to physical findings.

Various laboratory changes appear but are unspecific. They can be summarized in the Laboratory Risk Indicator for Necrotizing Fasciitis score (LRINEC).[1] Intraoperative pathognomonic findings are dishwasher like edema caused by liquefactive tissue necrosis with foul fish-water-odor, easily separated fascial planes also called the “finger-test”, and thrombosed perforating vessels.

Radical surgical debridement of necrotic tissue and broad-spectrum intravenous antibiotic therapy are the corner stones of treatment of NF.[2] Recommendations for first-line antibiotic treatment consist of penicillin, clindamycin, and fluoroquinolone or aminoglycoside for Gram-negative bacteria.[3] Repeated debridement may be required. Patients usually require intensive care support and management of multiorgan failure.

NF is caused by either type I or type II infections. Type I consists of poly-microbial anaerobic and facultative anaerobic bacteria and usually occur after surgical procedure in older patients. Type II is a mono-bacterial infection with Group A beta-hemolytic streptococcus, less frequently by other streptococci or staphylococci. This infection can also occur in younger patients and shows rapid progression. New classifications that are not widely used yet suggest an additional group with mono-bacterial gram-negative NF (MB-GN NF).[4]

We noticed an increase of cases with MB-GN NF with *Escherichia coli* (*E. coli*) over a one-year period.

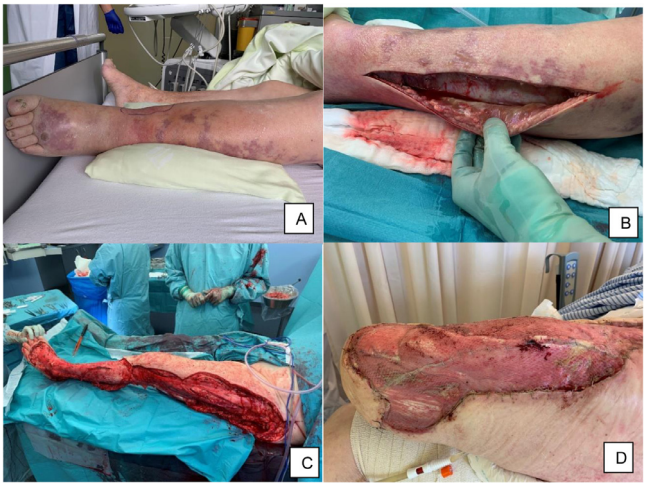

Fig. 1. Landscape-like necrosis (A), intraoperative findings (B), post radical debridement (C)and post-amputation and skin grafting (D)

Case series

Case 1

A 76-year-old man presented with a history of two days of fever, redness, swelling, and tenderness on palpation on the left lower leg. Because of deterioration under antibiotic treatment and suspicion of NF, the patient was admitted. The patient presented with septic shock and local findings consisted of typical findings for NF (Fig. 1A). The leg was swollen because of lymphedema and showed several chronic wounds. The patient received a debridement of the necrotic soft tissue. Intraoperative findings confirmed the diagnosis (Fig. 1B). After serial debridement and amputation at the level of the thigh (Fig. 1C-D), the patient became hemodynamically stable. The patient had a quick recovery but died six months later because of metastatic prostate cancer.

Case 2

A 69-year-old man presented with septic shock, redness, and pain out of proportion and landscape-like necrosis on the left foot. Because of Lymphoma the patient was under immunotherapy. NF was suspected and the patient received a debridement (Fig. 2A). On postoperative day 5, a partial secondary wound closure and skin grafting (Fig. 2B) could be performed and the patient was discharged. The patient died three months later because of catheter-associated sepsis with coagulase-negative staphylococcus causing endocarditis.

Case 3

A 78-year-old lady was treated with a laparoscopic hysterectomy and adnexectomy for cervix carcinoma. One day after the patient was discharged, she was referred to the emergency room with massive pain on the right hemi thorax and both lower extremities. Clinical findings consisted of septic shock, pain out of proportion on the right hemi-thorax and both lower extremities, crepitation, and landscape-like skin necrosis (Fig. 3A). Intra-abdominal infection was ruled out. The patient was debrided extensively on both lower extremities and the right hemi-thorax (Fig. 3B) but remained in septic shock. A further debridement was performed. Even with maximal intensive care treatment, the patient further deteriorated and died the same day of multiorgan failure.

Fig. 2. Post-radical debridement (A) and post skin grafting (B)

Fig. 3. Landscape-like necrosis and initial incisions (A) and initial debridement (B)

Case 4

A 57-year-old woman with a history of liver cirrhosis and hepatocellular carcinoma presented with progressive ascites. An aspiration of her ascites was performed. After the ascites aspiration, she deteriorated quickly and presented with tenderness and redness at the area of aspiration as well as

landscape like necrosis and septic shock. An extensive debridement was performed immediately and antibiotic treatment was escalated but the patient died the same day.

Results

We report four cases of MB-GN NF caused by *E. coli*. The patients had an average age of 70 years. All patients presented in septic shock, showed landscape-like skin necrosis and pain out of proportion (Table 1). One patient had fever and another one had crepitation as additional clinical finding. Three out of four cases showed a normal leucocyte count and one had leucopenia. All patients had elevated levels of CRP. Lactate was elevated in the cases with a poor short-term outcome. The LRINEC-score reached the cut off of six in two patients. All *E. coli* found in the samples were sensitive to the initial antibiotic treatment including amoxicillin clavulanic acid. Radical debridement and escalation of antibiotic treatment was performed in all patients immediately. Two patients had a favorable short-term outcome. Amputation or split thickness skin grafting led to coverage of the defect. They had a poor long time survival as both patients died within six months. Two patients did not respond to treatment and died of multiorgan failure. All patients had positive blood samples and soft tissue samples for *E. coli*. The histology taken was compatible with NF. All patients had a known oncologic diagnosis. One patient had in addition end stage renal disease and another one had liver cirrhosis.

Discussion

Type I and type II NF are well known. Recent findings suggest adding a type III fasciitis which is caused by monobacterial gram-negative organisms in up to 15% of NF.[4] In monobacterial NF alone Yahav found 47.4 % of monobacterial gram-negative organisms of which 52.6 % was caused by *E. coli*.[5]

A high suspicion for NF should be raised in patients with sepsis, landscape-like necrosis of the skin and pain out of proportion. The LRINEC-score does not seem to be very adequate for MB-GN NF as patients often present with normal white blood cell count or leucopenia.

It is documented that *E. coli* NF in hematological patients who had recent surgery on underlying malignancy or are immunosuppressed have a worse outcome[6-9] and there is a predominance of MB-GN NF in patients with liver cirrhosis.[10]

Usually NF is caused by bacteria entering the subcutaneous tissue through a wound where bacteria spread along the deep fascial planes and along the septum. This was the case in two of our patients. In two patients, the port of entry was either caused by laparoscopy or ascites aspiration. We postulate that in patients with MB-GN NF and oncologic diseases, liver cirrhosis, renal diseases, otherwise immunocompromised, or previous abdominal surgery hematogenous spreading is the cause of development of NF. In these patients, radical debridement is of limited use as the source of the bacterial seeding cannot be eliminated. This could explain the high initial mortality of 50% compared to published figures of 28 % over all mortality.[4]

In underlying diseases like liver cirrhosis, oncologic diseases, and renal diseases in addition to the normal empirical antibiotic regimes, MB-GN NF should be suspected and adequate empiric Gram-negative antibiotic cover added. However, even with adjusted antibiotic treatment and radical debridement, the short-term survival and long-term outcome are poor because of the underlying disease and potential hematogenous disseminated spreading.

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None

Conflicts of interest

None declared

Ethical approval

Not required

Table 1
S=Shock, F=Fever, P=Pain, B=Bullae, Land mark pattern necrosis=L, C=Crepitation

Case Sex Age	Localization	Laboratory findings and LRINEC-Score	Blood samples, Tissue samples, Histology	Co-Morbidities	Suspected port of entry	Symptoms	Time to intervention (h)	Initial antibiotic treatment/ Sensitive	Final antibiotic treatment	Outcome
1 M 76	Left lower leg and foot	WBC 4.4 G/L CRP 362 mg/L Hb 6.7 g/dL Na 141 mEq/L Crea 1.7 mg/dL Glucose 4.28 mmol/L Lactate 1.1 mmo/L LRINEC-Score 8	*E. coli* *E. coli* Compatible with NF	Metastatic prostate cancer, Lymphedema	Chronic leg ulcer	S,F,P,L	3	Amoxicillin clavulanic acid/yes	Piperacillin-tazobactam	Responding to debridement. Through the knee amputation. Death after 6 months.
2 M 69	Left foot	WBC 4.4 G/l CRP 143 mg/L Hb11.7 g/dL Na 131 mEq/L Crea 2.1 mg/dL Glucose 7.2 mmol/L Lactate 1.5 mmo/L LRINEC-Score 5	*E. coli* *E. coli* Compatible with NF	Lymphoma, Sub-Illeus, Heart insufficiency, Chronic renal insufficiency,	Chronic leg ulcer	S,P,L	3	Amoxicillin clavulanic acid/yes	Piperacillin-tazobactam and clindamycin	Responding to debridement. Split-thickness skin graft. Death after 3 months.
3 F 78	Right abdomen and both lower extremities	WBC 0.53 G/L CRP 101 mg/L Hb 9.4 g/dL Na 130 mEq/L Crea 1.12 mg/dL Glucose 1.7 mmol/L Lactate 8.1 mmo/L LRINEC-Score 4	*E. coli* *E. coli* Compatible with NF	Cervical cancer	Laparoscopy or liver cirrhosis	S,P,L,C	3	Piperacillin-tazobactam and clin-damycin/yes	Piperacillin-tazobactam and clindamycin	Non-Responding to debridement, Death at day 1.
4 F 57	Abdomen and flanks	WBC 7.3 G/L CRP 283 mg/L Hb 11.2 g/dL Na 132 mEq/L Crea 1.57 mg/dL Glucose 3.13 mmol/L Lactate 9.9 mmo/L LRINEC-Score 7	*E. coli* *E. coli* Compatible with NF	Liver cirrhosis, Hepatocellular carcinoma, Hepatitis C, Vasculitis	Ascites puncture	S,P,L	1	Ceftriaxone and clarithromycin/ yes	Piperacillin-tazobactam	Non-Responding to debridement, Death at day 1.

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