Received: 4 October 2022 | Revised: 16 November 2022 | Accepted: 3 January 2023

DOI: 10.1002/ccr3.6873

CASE REPORT

Clinical Case Reports Open Access WILEY

Bilateral non-contiguous necrotizing fasciitis of the lower extremities

Sascha T. Bender | **Maximilian Ganz** | **Peter R. Mertens** | **Christian Gross**

Clinic for Nephrology and Hypertension, Diabetes and Endocrinology, Otto-von-Guericke University Magdeburg, Magdeburg, Germany

Correspondence
Sascha T. Bender, Clinic for Nephrology and Hypertension, Diabetes and Endocrinology, Otto-von-Guericke University Magdeburg, Leipziger Str. 44, 39120 Magdeburg, Germany.
Email: sascha.bender@med.ovgu.de

Abstract

Necrotizing fasciitis (NF) is an uncommon soft tissue infection. Multifocal-extremity NF is a rarity with high mortality rates. Herein we report a case of bilateral non-contiguous NF of the lower extremities due to *Escherichia coli* with a fatal outcome, stressing the necessity of rapid and aggressive intervention in suspected cases.

KEYWORDS

bilateral, immunoglobulins, multifocal, necrotizing fasciitis

1 | INTRODUCTION

The term necrotizing fasciitis (NF) describes a group of rare, but potentially life-threatening invasive bacterial infections of the skin and subcutaneous soft tissues, which tend to progress fast along the fascia, causing fulminant tissue destruction. Pathomechanistically NF is characterized by synergistic effects of bacterial virulence factors (toxins, enzymes) and a disorder in the humoral immune defense of susceptible hosts, leading to intravascular thrombosis and ischemic necrosis.[1] The incidence has been reported to be 0.4–1.3/100,000 population, which has been observed rising in recent decades.[2]

2 | CASE PRESENTATION

A 65-year-old immunocompromised man, due to combined heart and kidney transplantation and a known diabetes mellitus type 2, was admitted to the intensive care unit with sepsis due to abscess formation following surgical repair of abdominal herniation.

The postoperative status of the patient was precarious with increasing need of hemodynamic support. Noradrenaline infusion up to 0.889 μg/kg/min in addition to fluid administration was required and argipressin at a dosage of 0.02 IE/min was necessary to achieve hemodynamic stabilization. Body temperature was measured 39.1°C and the heart rate at 115 bpm. Laboratory data are described in Table 1. On physical examination, the left limb showed a dusky purplish gangrenous-altered skin with ecchymosis, ruptured violaceous bullae and skin sloughing (Figure 1A). Palpating the edematous skin revealed distinct tenderness and crepitation. Within an hour the skin alterations spread rapidly onto nearly the complete left leg.

Blood cultures were positive with *Escherichia coli*. A subsequent computed tomography scan depicted gas in the subcutaneous tissue (Figure 1B, arrows). A clinical diagnosis of NF was made and immediate surgical intervention with aggressive epifascial necrosectomy of devitalized tissue and broad-spectrum antibiotic therapy, including meropeneme 1000 mg every 8 h and linezolide 600 mg twice daily, was administered. In addition

TABLE 1 Laboratory data

Variable	Reference range, adults	On arrival, ICU	12 h after arrival, after 1st operation	After 2nd operation, hospital day 3	Hospital day 5
Hemoglobin (mmol/L)	8.4–10.9	5.6	5.5	5.5	5.3
Hematocrit (%)	36.0–46.0	27	27	25	27
White-cell count (per µl)	3700–9800	1620	7920	6410	8600
Platelet count (per µl)	146,000–328,000	83,000	45,000	44,000	35,000
Sodium (mmol/L)	136–145	140	140	137	136
Potassium (mmol/L)	3.4–4.9	3.86	4.78	5.52	4.89
Glucose (mmol/L)	4.11–5.89	8.66	9.85	12	7.42
Creatinine kinase (µmol/L)	<3.2	1.05	0.73	0.31	0.24
C-reactive protein (mg/L)	<5	109	294	380	273
Procalcitonine (ng/ml)	<0.5	56	>100	>100	38
Creatinine (µmol/L)	59–104	216	174	173	106
Urea nitrogen (mmol/L)	3.0–9.2	37	27	22	12
Lactate (mmol/L)	<2.2	3.2	3.7	3.5	2.5
Albumin (g/L)	35–52	27	16.8	19.4	26.1
Aspartate aminotransferase (µmol/L)	0.17–0.85	0.22	0.40	0.25	0.22
International normalized ratio	<1.15	68	45	68	91
Activated partial thromboplastin time (s)	<34.4	34	45	68	94
pH	7.37–7.45	7.20	7.25	7.32	7.27

Abbreviation: ICU denotes intensive care unit.

high-dose (5 mg/mL plasma) intravenous polyspecific immunoglobulin G (IVIG) was dispensed. Histological work-up depicted an extensive acute neutrophilic inflammatory reaction involving the subcutaneous fat and severe necrosis. On the first postoperative day after radical debridement of the left limb (Figure 1C), similar skin alterations developed on the right crus (Figure 1D). A second debridement of the right leg was conducted. The clinical status of our patient deteriorated hereafter rapidly and he succumbed in the course of this severe invasive infection.

3 | DISCUSSION

Mortality rates with NF are reported to approximate 20% and remain high despite maximum therapy.[3] Severe systemic toxicity occurs more often in patients with older age, immunosuppression, diabetes, malignancy or chronic kidney disease.[3] The two most important risk factors associated with increased mortality are delay in surgery and extent of the first debridement.[4–6] Other risk factors associated with higher mortality rates are summarized in Table 2.

Common clinical findings include soft tissue edema, tenderness, blisters, bullae formation and a characteristic disproportionate local pain in early stages with transition to pathognomonic skin necrosis with dusky discoloration and crepitus in late stages, which are accompanied by systemic symptoms of shock.[7] Wong et al. established a laboratory-based scoring system to help discriminate between necrotizing and non-necrotizing infections, but with its lack of clinical parameters diagnosis cannot be ensured (Table 3).[8,9] Imaging studies contribute to the diagnosis of NF by detecting gas formation in soft tissues. But since there are no specific laboratory markers and radiological proof becomes only available in progressive disease, clinical suspicion is the main clue to the diagnosis of NF.

Bilateral NF is an atypical presentation. Concomitant or secondary involvement of remote sites is defined as multifocal NF (MNF) and has been reported in only few cases.[10,11] In a recent study by Lee et al. only 5% of all cases specified as MNF.[12] Development of new lesions at distant sites might be caused by either hematogenous dissemination, simultaneous colonization or direct spreading.[12,13] Time lag in manifestation of a subsequent lesion might hint to the underlying mechanism.[11] Overall mortality rates of patients presenting with MNF doubles, ranging between 62% and 67%.[12]

The most likely etiology in this case is the abdominal septic abscess formation, leading to metastatic distribution

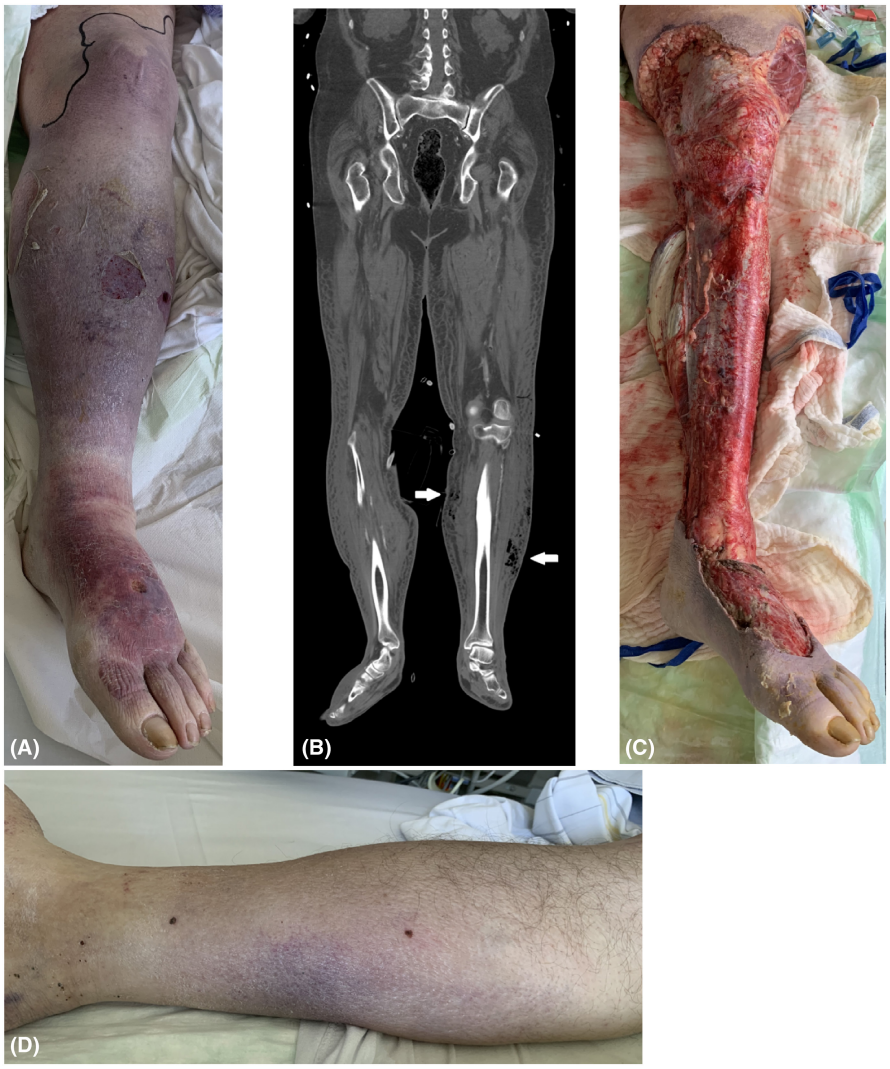

FIGURE 1 (A) Late Stage Necrotizing Fasciitis. The left leg showing edematous altered skin with a dusky purplish discoloration and ruptured violaceous bullae. (B) Computed tomography scan of the same leg revealing free air in soft tissue (arrows). (C) Postoperative image after radical debridement and necrosectomy. (D) Progressive necrotizing fasciitis of the right crus displayed livid discoloration and edematous swelling on day 2

of *E. coli* via the blood flow to multiple sites. Our case is particularly rare therein that NF due to *E. coli* manifests in a multifocal fashion. Such a fulminant presentation of symptoms and progressive disease course is likely because of the compromised immune status of the patient following organ transplantation. This overall situation may also interfere with the laboratory risk indicator for necrotizing fasciitis-score. This fatal outcome emphasizes the urgent necessity of early and aggressive intervention, especially in cases of MNF.

Hallmark for a successful management of NF is immediate extended surgical debridement of all affected tissues. Concomitantly initiation of broad-spectrum antibiotic coverage e.g. with piperacillin/tazobactam to also address anaerobic bacteria plus clindamycin as soon as NF is suspected is essential.

Adjuvant therapeutic approaches may include administration of intravenous immunoglobulins, especially in the early disease course and in the setting of streptococcal infection belonging to group A.[14–16] In the index case IVIG was administered because of proven immunoglobulin deficiency (IgG 3.07 [7–16] g/L) in the immunocompromised patient. Hyperbaric oxygen therapy (HBOT) as another adjunctive therapeutic option is discussed controversially.[17,18] We did not implemented HBOT in this case, since we lacked the possibility for a pressure chamber with affiliated intensive care capacity. Moreover transportation risks for our patient were assessed to be too high at the time.

4 | CONCLUSION

Necrotizing fasciitis diagnosis is often delayed because of the lack of specific clinical features in the initial stage of the disease. Clinicians should be aware of NF as differential diagnosis especially if there are indications of soft tissue infection combined with signs of systemic involvement. NF might rarely present in a multifocal manner, which tends to have an even more unfavorable outcome.

TABLE 2 Predicting factors for higher mortality rates in patients with necrotizing fasciitis[19–26]

Delay in surgery, especially >24 h
Extent of first debridement
Septic condition with hypotension at time of admission • Elevated lactate levels • White-cell count >30,000 per µl • Bacteremia
Comorbidities • Chronic renal failure • Heart disease • Cirrhosis • Peripheral vascular disease
Acute kidney injury • Serum creatinine >177 mmol/L • Elevated blood urea • Systemic acidosis
Increased serum creatine kinase
Decreased international normalized ratio
Deceased albumin levels
Low hematocrit
Older age > 50 years
Infection sites apart from extremities
Multifocal necrotizing fasciitis

TABLE 3 LRINEC-score (Laboratory Risk Indicator for NECrotizing Fasciitis)[8]

Variable	Value	Score	Point value, patient
Hemoglobin (g/dl)	11–13.5 <11	1 2	2
White-cell count (per µl)	15,000–25,000 >25,000	1 2	0
Sodium (mmol/L)	<135	2	0
Creatinine (µmol/L)	>141	2	2
Glucose (mmol/L)	>10	1	0
C-reactive protein (mg/L)	>150	4	0
LRINEC score			
≤5 points: low risk			4
6–7 points: medium risk			
≥8 points: high risk			

AUTHOR CONTRIBUTIONS

Sascha T. Bender: Conceptualization; resources; writing – original draft; writing – review and editing. **Peter R. Mertens:** Supervision; writing – review and editing. **Christian Gross:** Data curation; supervision; writing – original draft.

ACKNOWLEDGMENTS

None. Open Access funding enabled and organized by Projekt DEAL.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

DATA AVAILABILITY STATEMENT

Data sharing not applicable.

CONSENT

Written consent has been obtained from the patient.

ORCID

Sascha T. Bender https://orcid.org/0000-0002-8946-1174

REFERENCES

1. Misiakos EP, Bagias G, Patapis P, Sotiropoulos D, Kanavidis P, Machairas A. Current concepts in the management of necrotizing fasciitis. *Front Surg*. 2014;1:36. doi:10.3389/fsurg.2014.00036
2. Soltani AM, Best MJ, Francis CS, Allan BJ, Askari M, Panthaki ZJ. Trends in the incidence and treatment of necrotizing soft tissue infections: an analysis of the National Hospital Discharge Survey. *J Burn Care Res*. 2014;35(5):449-454. doi:10.1097/BCR.0000000000000010
3. Golger A, Ching S, Goldsmith CH, Pennie RA, Bain JR. Mortality in patients with necrotizing fasciitis. *Plast Reconstr Surg*. 2007;119(6):1803-1807. doi:10.1097/01.prs.0000259040.71478.27
4. Wong CH, Chang HC, Pasupathy S, Khin LW, Tan JL, Low CO. Necrotizing fasciitis: clinical presentation, microbiology, and determinants of mortality. *J Bone Joint Surg Am*. 2003;85(8):1454-1460.
5. Mok MY, Wong SY, Chan TM, Tang WM, Wong WS, Lau CS. Necrotizing fasciitis in rheumatic diseases. *Lupus*. 2006;15(6):380-383. doi:10.1191/0961203306lu2314cr
6. Bucca K, Spencer R, Orford N, Cattigan C, Athan E, McDonald A. Early diagnosis and treatment of necrotizing fasciitis can improve survival: an observational intensive care unit cohort study. *ANZ J Surg*. 2013;83(5):365-370. doi:10.1111/j.1445-2197.2012.06251.x
7. Wang YS, Wong CH, Tay YK. Staging of necrotizing fasciitis based on the evolving cutaneous features. *Int J Dermatol*. 2007;46(10):1036-1041. doi:10.1111/j.1365-4632.2007.03201.x
8. Wong CH, Khin LW, Heng KS, Tan KC, Low CO. The LRINEC (Laboratory Risk Indicator for Necrotizing Fasciitis) score: a tool for distinguishing necrotizing fasciitis from other soft tissue infections. *Crit Care Med*. 2004;32(7):1535-1541. doi:10.1097/01.ccm.0000129486.35458.7d
9. Borschitz T, Schlicht S, Siegel E, Hanke E, von Stebut E. Improvement of a clinical score for necrotizing fasciitis: "pain out of proportion" and high CRP levels aid the diagnosis. *PLoS One*. 2015;10(7):e0132775. doi:10.1371/journal.pone.0132775

10. El-Khani U, Nehme J, Darwish A, et al. Multifocal necrotising fasciitis: an overlooked entity? *J Plast Reconstr Aesthet Surg*. 2012;65(4):501-512. doi:10.1016/j.bjps.2011.09.001
11. Tocco I, Lancerotto L, Pontini A, Voltan A, Azzena B. "Synchronous" multifocal necrotizing fasciitis. *J Emerg Med*. 2013;45(6):e187-e191. doi:10.1016/j.jemermed.2013.05.064
12. Lee CY, Li YY, Huang TW, et al. Synchronous multifocal necrotizing fasciitis prognostic factors: a retrospective case series study in a single center. *Infection*. 2016;44(6):757-763. doi:10.1007/s15010-016-0932-9
13. Fukuda K, Ryujin M, Sakio R, Fukuzumi S, Omae T, Hayakawa K. Bilateral necrotizing fasciitis of the foot associated with group B streptococcus. *Case Rep Dermatol*. 2016;8(3):243-249. doi:10.1159/000448163
14. Babbar A, Bruun T, Hyldegaard O, et al. Pivotal role of preexisting pathogen-specific antibodies in the development of necrotizing soft-tissue infections. *J Infect Dis*. 2018;218(1):44-52. doi:10.1093/infdis/jiy110
15. Bruun T, Rath E, Madsen MB, et al. Risk factors and predictors of mortality in streptococcal necrotizing soft-tissue infections: a multicenter prospective study. *Clin Infect Dis*. 2021;72(2):293-300. doi:10.1093/cid/ciaa027
16. Parks T, Wilson C, Curtis N, Norrby-Teglund A, Sriskandan S. Polyspecific intravenous immunoglobulin in clindamycin-treated patients with streptococcal toxic shock syndrome: a systematic review and meta-analysis. *Clin Infect Dis*. 2018;67(9):1434-1436. doi:10.1093/cid/ciy401
17. Riseman JA, Zamboni WA, Curtis A, Graham DR, Konrad HR, Ross DS. Hyperbaric oxygen therapy for necrotizing fasciitis reduces mortality and the need for debridements. *Surgery*. 1990;108(5):847-850.
18. Mindrup SR, Kealey GP, Fallon B. Hyperbaric oxygen for the treatment of fournier's gangrene. *J Urol*. 2005;173(6):1975-1977. doi:10.1097/01.ju.0000158129.56571.05
19. Martinschek A, Evers B, Lampl L, Gerngroß H, Schmidt R, Sparwasser C. Prognostic aspects, survival rate, and predisposing risk factors in patients with Fournier's gangrene and necrotizing soft tissue infections: evaluation of clinical outcome of 55 patients. *Urol Int*. 2012;89(2):173-179. doi:10.1159/000339161
20. Clayton MD, Fowler JE, Sharifi R, Pearl RK. Causes, presentation and survival of fifty-seven patients with necrotizing fasciitis of the male genitalia. *Surg Gynecol Obstet*. 1990;170(1):49-55.
21. Rea WJ, Wyrick WJ. Necrotizing fasciitis. *Ann Surg*. 1970;172(6):957-964. doi:10.1097/00000658-197012000-00005
22. Sorensen MD, Krieger JN, Rivara FP, Klein MB, Wessells H. Fournier's gangrene: management and mortality predictors in a population based study. *J Urol*. 2009;182(6):2742-2747. doi:10.1016/j.juro.2009.08.050
23. Green RJ, Dafoe DC, Raffin TA. Necrotizing fasciitis. *Chest*. 1996;110(1):219-229. doi:10.1378/chest.110.1.219
24. Anaya DA, McMahon K, Nathens AB, Sullivan SR, Foy H, Bulger E. Predictors of mortality and limb loss in necrotizing soft tissue infections. *Arch Surg*. 2005;140(2):151-157; discussion 158. doi:10.1001/archsurg.140.2.151
25. Huang KF, Hung MH, Lin YS, et al. Independent predictors of mortality for necrotizing fasciitis: a retrospective analysis in a single institution. *J Trauma*. 2011;71(2):467-473; discussion 473. doi:10.1097/TA.0b013e318220d7fa
26. Hua C, Sbidian E, Hemery F, et al. Prognostic factors in necrotizing soft-tissue infections (NSTI): a cohort study. *J Am Acad Dermatol*. 2015;73(6):1006-1012.e8. doi:10.1016/j.jaad.2015.08.054

How to cite this article: Bender ST, Ganz M, Mertens PR, Gross C. Bilateral non-contiguous necrotizing fasciitis of the lower extremities. *Clin Case Rep*. 2023;11:e06873. doi:10.1002/ccr3.6873