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Case report

Intravenous immunoglobulin in necrotizing fasciitis – A case report and review of recent literature

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HIGHLIGHTS

- Necrotizing fasciitis (NF) is an inflammatory disease, which causes local tissue destruction up to lethal septic shock.
- We describe the case of a 33-year-old male patient representing an NF of his left leg.
- After non-responding to established broad anti-infective treatment, the patient received immunoglobulin (IVIg).
- The presented case suggests that IVIg treatment of patients with NF might be considered in case of critically ill patients.

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ABSTRACT

Introduction: Necrotizing fasciitis (NF) is an inflammatory disease of the soft tissue, which causes local tissue destruction and can lead to lethal septic shock. The therapy consists of early surgical treatment of the septic focus and an accompanying broad spectrum antibiotic therapy. Recent literature considers the additional use of immunoglobulin therapy in severe soft skin and tissue infections.
Presentation of case: In this report, we describe the case of a 33-year-old male patient treated at a university hospital intensive care unit because of an NF of his left leg. The patient rapidly developed a complicated septic disease after a minor superficial trauma. Despite intense microbiological diagnosis, no causative pathogens were identified. After non-responding to established broad anti-infective treatment, the patient received intravenous immunoglobulin, that rapidly improved his clinical condition.
Discussion: NF represents a disease processes, which is characterized by fulminant, widespread necrosis of soft tissue, systemic toxicity, and high mortality (>30%). Beside the surgical debridement and broad spectrum antibiotic therapy IVIg therapy might be an additional option in the treatment of NF. But the current literature supporting the use of IVIG in NF is largely based on retrospective or case-controlled studies, and only small randomized trials.
Conclusion: The demonstrated case suggests that IVIg treatment of patients with NF can be considered in case of hemodynamic unstable, critically ill patients. Although randomized controlled trials are missing, some patients might benefit from diminishing hyperinflammation by immunoglobins.

1. Introduction

Necrotizing fasciitis (NF) is defined as a rapidly expanding infection of fascia and subcutaneous tissue [1]. In general, the NF can occur ubiquitously in soft tissues, but most common areas of expansion are the extremities and in particular the lower legs [2]. Even trunk, abdomen, head, neck area, or anal region are often infected after surgery [3]. Common triggers are trivial trauma, burns, surgery, decubital ulcers, perirectal abscesses or Fournier's gangrene [4]. Risk factors for NF include diabetes mellitus, immunosuppression, malnutrition, age, intravenous drug misuse, peripheral vascular disease, renal failure, malignancy, and obesity [5]. Patients with NF usually present severe pain around the affected area and signs of skin infection (erythema, swelling, oedema, subcutaneous plaques, or surface nodes) [6]. These physical findings may rapidly evolve into a haemorrhagic infarction of the subcutis, the fascia and the dermis with the formation

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of areal, painless gangrene [6]. The NF is categorized into polymicrobial (type 1) and monomicrobial (type 2) infections [7]. Type 1 are mixed infections caused by anaerobic bacteria and Streptococci mainly serogroup A. Among these, *Staphylococcus aureus*, *Bacteroides fragilis* and anaerobic cocci are the most common pathogens [8]. Type 2 infections are caused by *Streptococcus pyogenes* alone, or in association with *S. aureus* or *Staphylococcus epidermidis*. Clostridial infections have been classified by some authors as type 3 necrotizing soft tissue infections [9]. Laboratory tests usually show pronounced leucocytosis associated with acidosis, hypocalcaemia, and anaemia [10]. The detection of pathogens should be established by blood cultures and biopsies of the affected areas. The mortality of NF is, depending on the study, up to 50% and is usually caused by a pronounced sepsis with secondary multi organ failure [11,12]. Because of the very rapid progression and high mortality, early diagnosis and effective therapy are needed [11,13]. In addition to the surgical treatment of the infection focus with repeated debridement of the affected area, intravenous administration of broad-spectrum antibiotics should be started early [2,13].

2. Presentation of case

A 33-year-old patient in good general health and nutritional status (185 cm, 80 kg) suffered from a minor, superficial injury on his lower left leg, which he acquired during a ski vacation. The patient had no pre-existing diseases and no significant medical history. Local self-treatment led to a deterioration of the wound conditions. About 10 days after the initial trauma, the outpatient visited the centre for general medicine, followed by the initiation of an antibiotic therapy with oral Cefuroxime. Because of a progressive clinical deterioration of the wound conditions with appearance of an aching hematoma, he was admitted two days later to hospital for surgical treatment of the hematoma. In the course of the next five days, two further wound debridements and the application of a vacuum-assisted closure were performed. The antibiotic therapy was escalated to Clindamycin (3×600 mg/d) and Tazobactam (3×4.5 g/d). Due to a recent clinical deterioration and the need for advanced therapeutic measures nine days after admission, the patient was transferred to a university hospital.

On hospital admission, the patient was awake, oriented and in stable respiratory and circulatory condition. During the clinical examination, his temperature was 37.2 °C, his blood pressure was 171/85 mmHg, pulse 140 beats per minute, rhythmic and his initial oxygen saturation checked by pulse oximetry was 95% in room air. He was somnolent but easily aroused and on examination presented. Secondary findings in physical examination were severe pain and swellings in both axillae and in both groins. A laboratory evaluation revealed an increase in white blood cell (WBC) count ($23.1 \times 10^3/\mu L$; reference value 4.00 to $11.00 \times 10^3/\mu L$), and C-reactive protein (CRP) 298.8 mg/dL (reference value 0.0–0.5 mg/dL). On the day of admission and the day after admission, we immediately performed surgical wound excisions with large debridement in the infected area of the left lower leg (Fig. 1). Due to international recommendations [14–16] and the current antibiotic guidelines at our hospitals intensive care unit (ICU), empirical antibiotic therapy was changed to Meropenem (4×1000 mg/d), Penicillin G (6x 5 Mega I.E./d) and Clindamycin (3×600 mg/d).

For further diagnostics, tissue samples and swabs from all infected areas were taken intraoperatively. Blood cultures were also taken at different time points. But no causative pathogen could be identified. Because of further increased inflammation markers and clinical deterioration, the anti-infective therapy was supplemented by Levofloxacin (2×500 mg/d) and Daptomycin (1000 mg loading-dose, 500 mg/d) for the coverage of *methicillin-sensitive S. aureus* and atypical pathogens two days after hospital admission. Caspofungin (70 mg loading-dose, 50 mg/d) was also added to cover invasive fungal infections. On the third day after admission, a hole-body computed tomography scan was performed. The result showed a fasciitis of the left upper and lower leg, and a symmetrical bilateral pulmonary oedema. Furthermore, bilateral pleural effusions impressed with basal atelectasis and a generalized barrier disruption. Because of a progredient lung oedema (Fig. 2) and consecutive respiratory dysfunction the patient developed the need for mechanical ventilation.

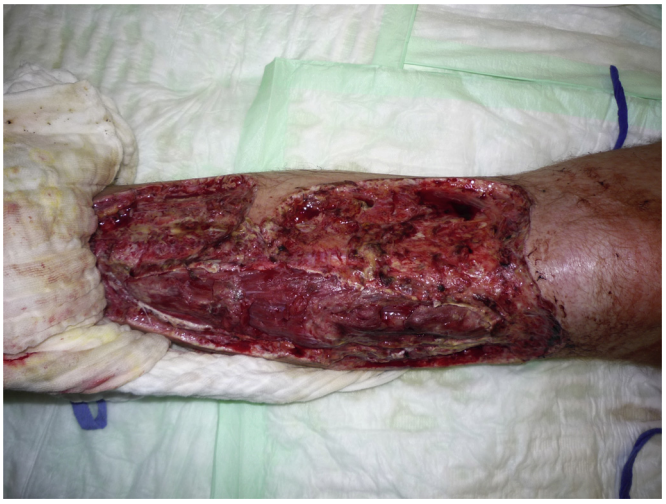

Fig. 1. Left lower leg at day 3 after admission.

At day 4 after admission, an additional operational inspection and large debridement of both axillae were performed. Additionally, the left thigh was surgically explored and a fasciotomy was performed. The intraoperative inspection of the left leg revealed a significant increase of the necrotic area. The microbiological analyses of the collected samples were all negative. Because of a positive serological evidence of *Herpes simplex virus-I* a therapy using Acyclovir (6×250 mg/d) was initiated. The following microbiological tests using polymerase chain reaction resulted in the detection of *Corynebacterium tuberculostearicum* in the taken wound swab, and *Acinetobacter baumanii* in wound swabs, tissue biopsy, pleural-punctate and blood. A direct detection of pathogens did not succeed at any time.

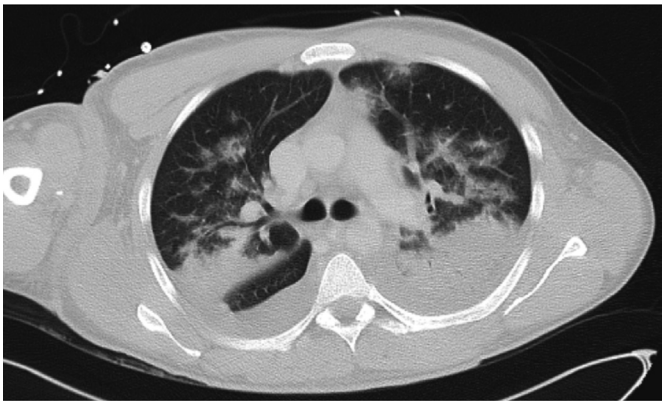

Fig. 2. CT Image at day 3 after admission showing lung oedema, pleural effusions, compression atelectasis of both lower lung lobes, and dorsal superior lobes. Ventilated areas showing focal and lobular oedema, and thickening of the interlobular septa.