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# Limb Salvage in Necrotizing Fasciitis

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## Abstract and Introduction

### Introduction

Necrotizing fasciitis (NF) is a life-threatening soft tissue infection caused by toxin-producing bacteria. It is a serious, alarming condition for the surgeons because of its propensity for extensive soft tissue destruction and high mortality rate. The infection can be associated with severe systemic toxicity and can rapidly progress to death unless recognized and treated promptly. Fortunately, this type of dermal gangrene is relatively rare in modern surgical practice. Presumably, antibiotics have helped to reduce the incidence of the disease. There is a five-fold increase in the incidence of the disease over the last few decades, which is largely unexplained, although increased longevity within the overall population and an increase in the number of immunosuppressed individuals may be two of the main causes.[1,2]

The disease was recognized by Hippocrates in the 5th century AD, who spoke of it as a complication of erysipelas.[3] The disease was first identified in 1848. In the United States, it was first described in 1871 by a Civil War surgeon who described cases of hospital gangrene. Meleney then identified and described the disease in 1920, but the term NF was introduced by Wilson in 1952. Since then, other terms have been used to refer to NF, including necrotizing soft tissue infection, streptococcal gangrene, gas gangrene, bacterial synergistic gangrene, hospital gangrene, flesh-eating bacteria syndrome, Clostridial myonecrosis, Meleney's synergistic gangrene, and Fournier's gangrene, the latter being specific to the involvement of scrotum and perineum in males. Although many different names have been used to describe the various NF, they often have a common pathology.[1,4,5]

Despite the improvements in critical care, antibiotics, and surgical technology, mortality still ranges between 30% and 50%.[2,4] In complicated cases like renal failure and multi-organ system failure, the mortality rate goes up to 70%.[6,7] Among patients with NF, the mortality rate is higher in patients with streptococcal toxic shock syndrome. Because large prospective studies have not been performed, the factors that contribute to mortality cannot be stated with certainty. The following are the possible prognostic factors that contribute to mortality: the duration of time from onset of infection to definitive treatment; the type, extent, and adequacy of surgical debridement; and infection of the head and neck, thorax, and abdomen, which are more complex in terms of surgical debridement. Other risk factors that have been shown to correlate with increased mortality include advanced age (> 50 years), diabetes mellitus, co-existing systemic sepsis and development of organ failure, arteriosclerosis, chronic renal insufficiency, congestive cardiac failure, and malnutrition.[7,8]

Two clinical types exist based on the organisms cultured from the wounds. Type I, or polymicrobial NF, is a mixed infection caused by aerobic and anaerobic bacteria. It occurs most commonly after surgical procedures, particularly after abdominal or perianal operations, and in patients with diabetes mellitus, peripheral vascular disease, and immunodeficiency syndrome. It can follow trauma, lung infection, dental extraction, cardiac catheterization, and usually no preceding history can be elicited, but there might be some easily forgotten trauma, such as minor laceration or insect bite. This form initially may be mistaken for a simple wound cellulitis. However, severe pain and systemic toxicity which reflect widespread tissue necrosis of underlying, apparently viable, skin apart from the wound site differentiate it from wound cellulitis. Type I NF is more often associated with diabetes mellitus, so NF should be considered in diabetic patients with cellulitis who also have systemic signs of infection, such as tachycardia leukocytosis marked by hyperglycemia or acidosis.

Although in Meleney's original series hemolytic streptococcus was isolated exclusively, no single microbe pathogenic for NF has ever been found. In type I NF, which is polymicrobial, a mixed infection is caused by aerobic and anaerobic gram-positive and gram-negative bacteria. Bacteria can be isolated from almost all cases of type I NF.9 The predominant isolates are *Staphylococcus aureus*, *Streptococci*, *Enterococci*, *Escherichia coli*, *Peptostreptococcus* species, Bacteroides fragilis group, *Clostridium* species, *Klebsiella*, and *Pseudomonas*. Type II NF refers to a monomicrobial infection caused by group A streptococcus (GAS, *Streptococcus pyogenes*).

Type II NF can occur at any age and among patients who do not have a complicated medical illness.[10] Predisposing factors include a history of blunt trauma, varicella (chickenpox), intravenous drug use, penetrating injury, and burns. Necrotizing fasciitis caused by group A streptococcus is frequently associated with toxic shock syndrome.[11] Some have also described type III NF, usually caused by Marine vibrio gram-negative rods.[12,13] Approximately 20% of cases occur without an obvious portal of entry, and are referred to as idiopathic NF. Idiopathic NF is more likely to occur in patients with few comorbid

medical problems, is typically caused by a single organism (*Streptococcus pyogenes*), and commonly involves the lower extremities. This condition is thought to be the result of infection from unrecognized breaks in the skin or from hematogenous spread.[9] The usual age is 38–45 years, but no age is immune for development of NF. Approximately one-half of the cases of streptococcal NF occur in young and previously healthy people. Male-female ratio is about 3:1. The US Centers for Disease Control and Prevention (CDC) estimates 500–1500 new cases are reported in the United States each year, but no data are available from developing countries.

The disease is rare in children, but when it occurs, it has a fulminant course with a high mortality rate. Poor socio-economic condition predisposes the children to NF, especially in developing countries.[14] The source of infection is genito-urinary tract (25%), anorectal (25%), intra-abdominal (10%), and unidentified source (40%).[15,16]

## Case Report

A 60-year-old man with a known case of diabetes mellitus (on oral hypoglycemics) was admitted into the surgery unit with pain and mild swelling of the distal part of the left thigh. It started as a small furuncle on the medial aspect of the left thigh.

After using traditional local preparation, the swelling and furuncle started to spread all over the thigh. Upon examination, his general condition was good. He was fully conscious, hemodynamically stable, and afebrile. His pulse was 90/min, BP 130/80 mmHg, and his temperature was 37.2°C (99°F). He had difficulty walking due to severe pain in the left lower extremity. Local examination of the left thigh showed a 6 cm x 8 cm area of minor erythema, moderate edema, and ecchymosis with dark reddish discoloration of skin, especially along the medial aspect. The thigh was oedematous and very tender on palpation. All laboratory parameters were within the normal range except RBS 13.2 mmol/L and TPC- 165000/$mm^3$. Urine analysis revealed sugar (+++) and acetone (++).

Medical consultation for the management of diabetes mellitus was ordered. The patient was diagnosed with a case of cellulitis of the left thigh and was put on an injection of Velosef 500 mg IV 6/h; Inj. Flagyl 500 mg IV 8/h; Inj. L/R 500 mL IV daily; Inj. normal saline 1000 mL IV daily; injected insulin according to sliding scale. A swab was taken from the blister for culture and sensitivity testing. On the second day of admission, the inflammation extended to the groin superiorly and to the knee joint inferiorly (Figure 1). The patient developed a similar dusky purple area of inflammation at about 10 cm x 6 cm in the left iliac fossa region. Over the next 12 hours, the patient developed tachycardia and tachypnea and became drowsy with sluggish responses to verbal commands. Diagnosis of NF was obvious and debridement was immediately performed under general anesthesia. The skin, subcutaneous tissue, and superficial and deep fascia of the medial, anterior, and posterior aspect of the thigh was debrided, sparing the lateral aspect of the thigh (Figure 2), and the lateral aspect of the thigh was gradually debrided. The general condition of the patient was critical after debridement and he was transferred to the ICU. Hemodynamically, the patient was stable but drowsy and responded only to deep, painful stimuli. He had a complicated course including tachycardia and thrombocytopenia. His pulse was 112/min; blood pressure 100/80 mmHg; temperature 37.2°C (99°F); SPO2 100% with mask oxygen. The patient's urine output was adequate. The wound swab culture showed growth of *Pseudomonas* and was sensitive to imipenem. The patient's treatment included fluid and electrolytes (L/R, DNS, N/S) 200 mL/h (successively reduced); antibiotics (Ing. Tienam 0.5 g IV, 6 hourly); analgesics; injection of Clexane 0.4 mL s/c daily; IVIG Inj. Albumin; blood transfusion; platelet concentrate and FFP; and a high-protein and diabetic diet. The patient was nursed on an air mattress and pressure-sore preventive measures were followed. Daily debridement and scraping of the wound was done, followed by normal saline washing and dressing with povidone iodine (diluted), fucidin ointment, sofra-tulle, and moist gauze. Gradually, the general condition of the patient improved and raw area in the anterior surface of the thigh and the left iliac fossa was fit for grafting. During the fourth wound debridement (30 days after the onset of disease), a split skin graft (manually meshed) was placed over the anterior surface of the left thigh and in the left iliac fossa (Figures 3a, b). After debridement, the rest of the bare area of the thigh was covered by split-skin grafting in four stages. The patient had undergone wound debridement on eight occasions during the hospitalization period. Skin was harvested from the right thigh, right buttock, right leg, and left leg. Graft take was very good and wound healing was satisfactory (Figures 4a, b). Following physiotherapy, the patient was ambulated and discharged 113 days after admission. He was put on pressure garments at the time of discharge to prevent hypertrophic scarring. The patient was reviewed in an outpatient clinic after one month and had no appreciable functional deformity. He returned to his normal work 6 months from the onset of the disease.

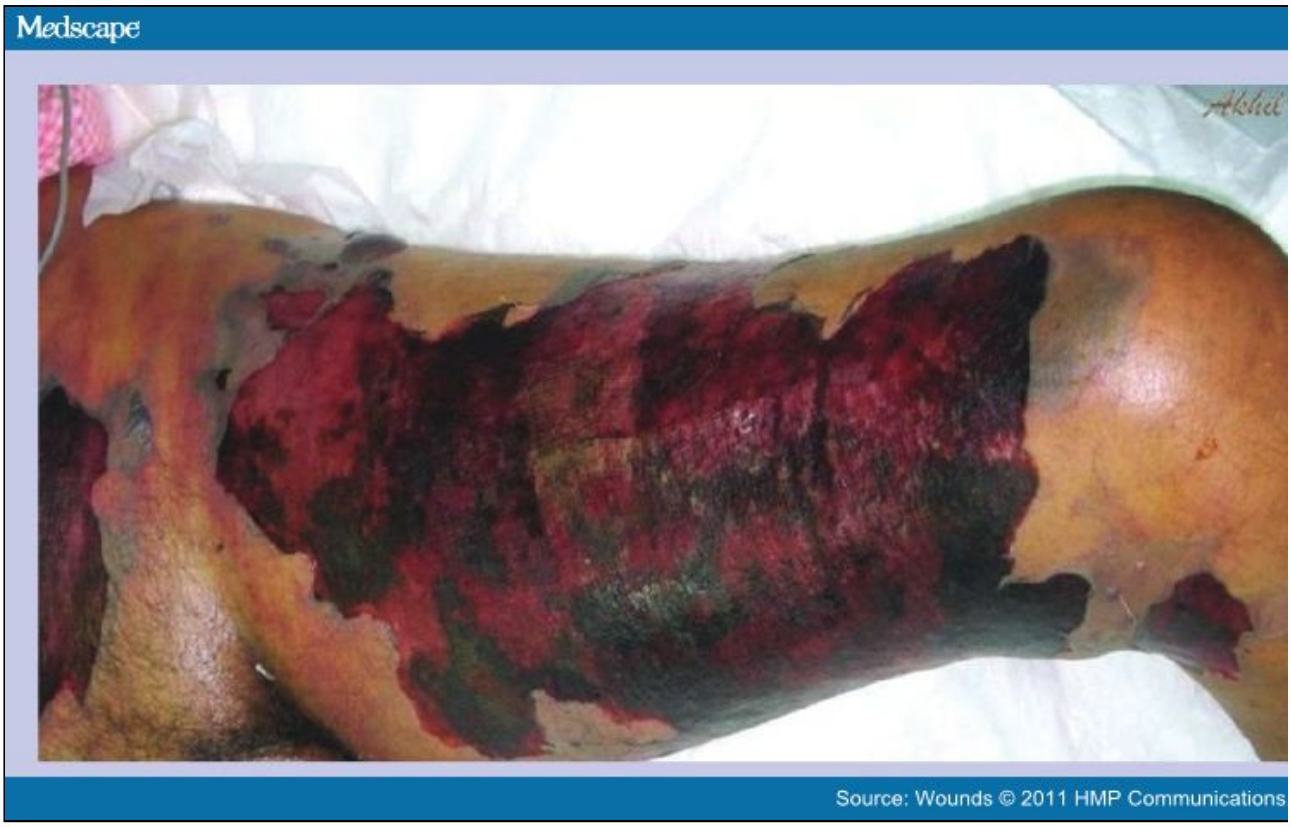


**Figure 1.** Inflammation extended to the groin superiorly and to the knee joint inferiorly.

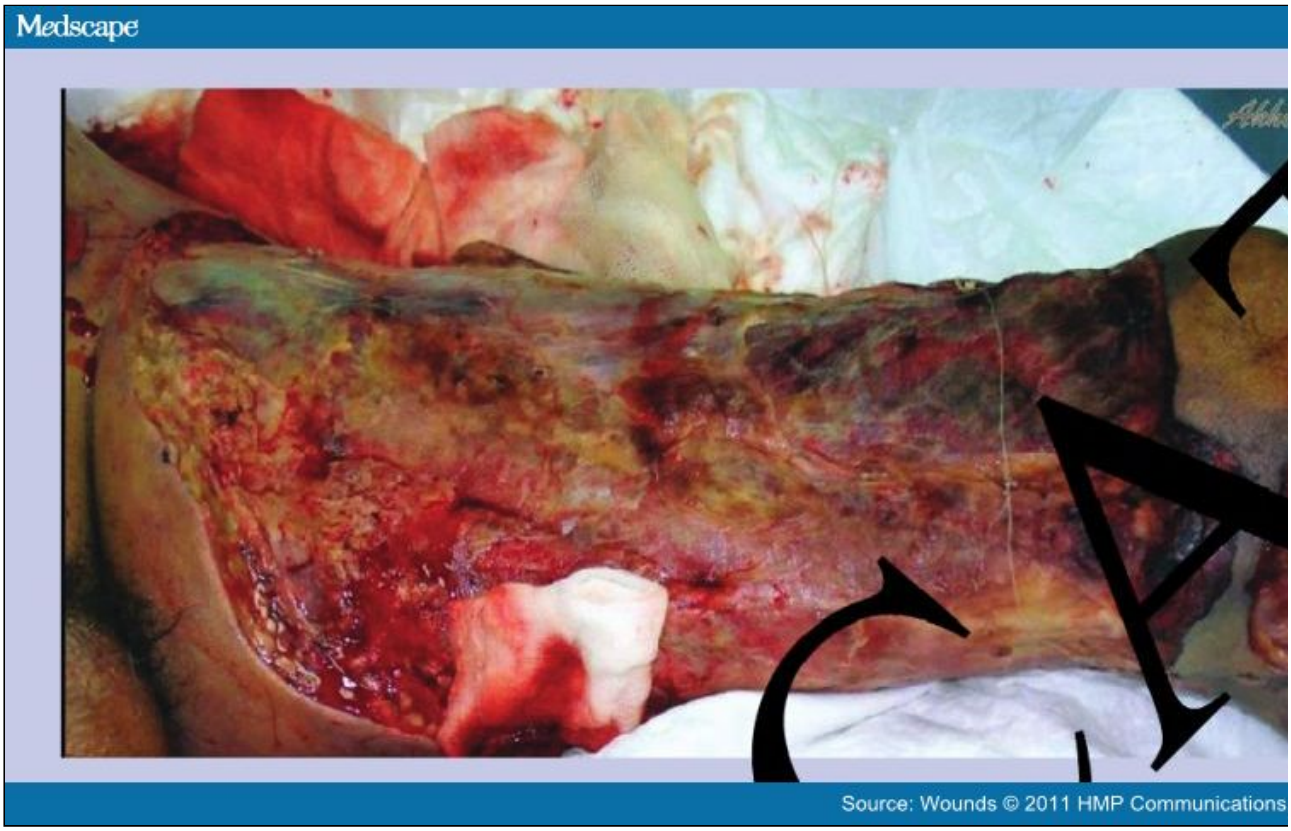


**Figure 2.** The medial, anterior, and posterior aspect of the thigh was debrided.

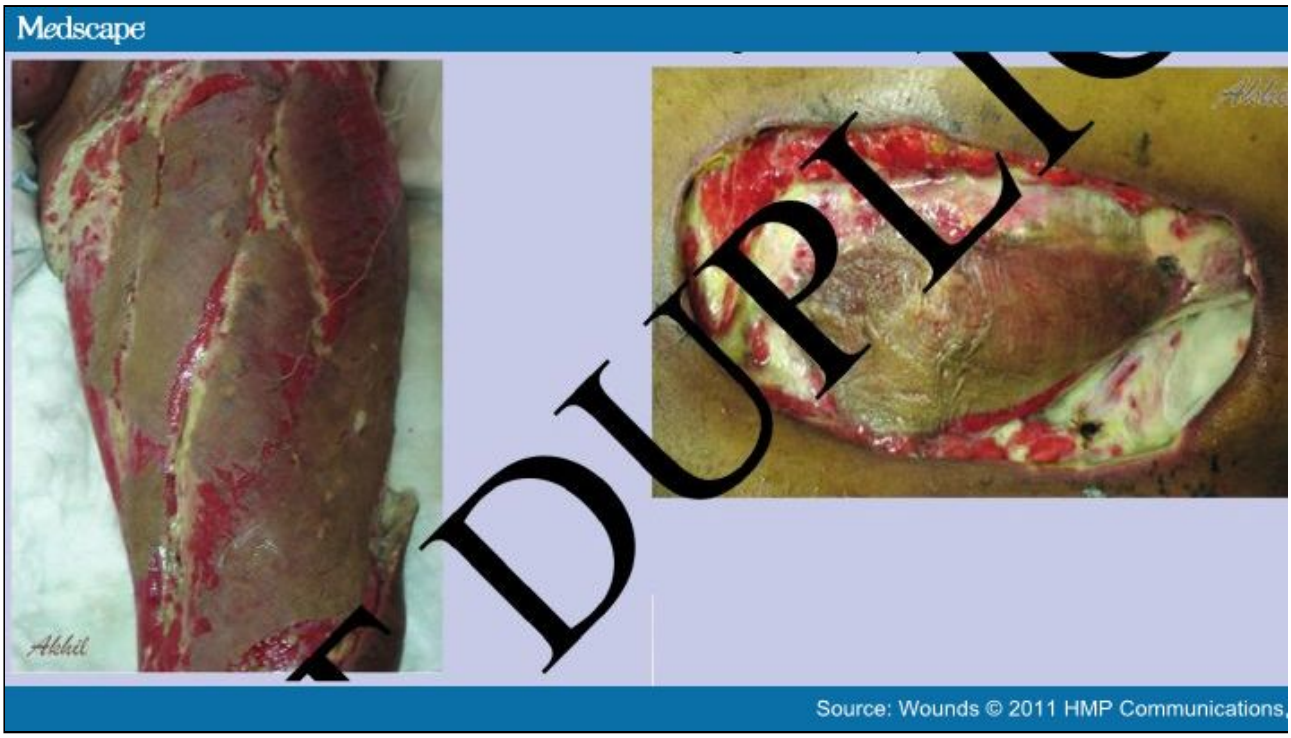


**Figure 3.** **a** Skin graft placed over the anterior surface of the left thigh. **b** Skin graft placed over the left iliac fossa.

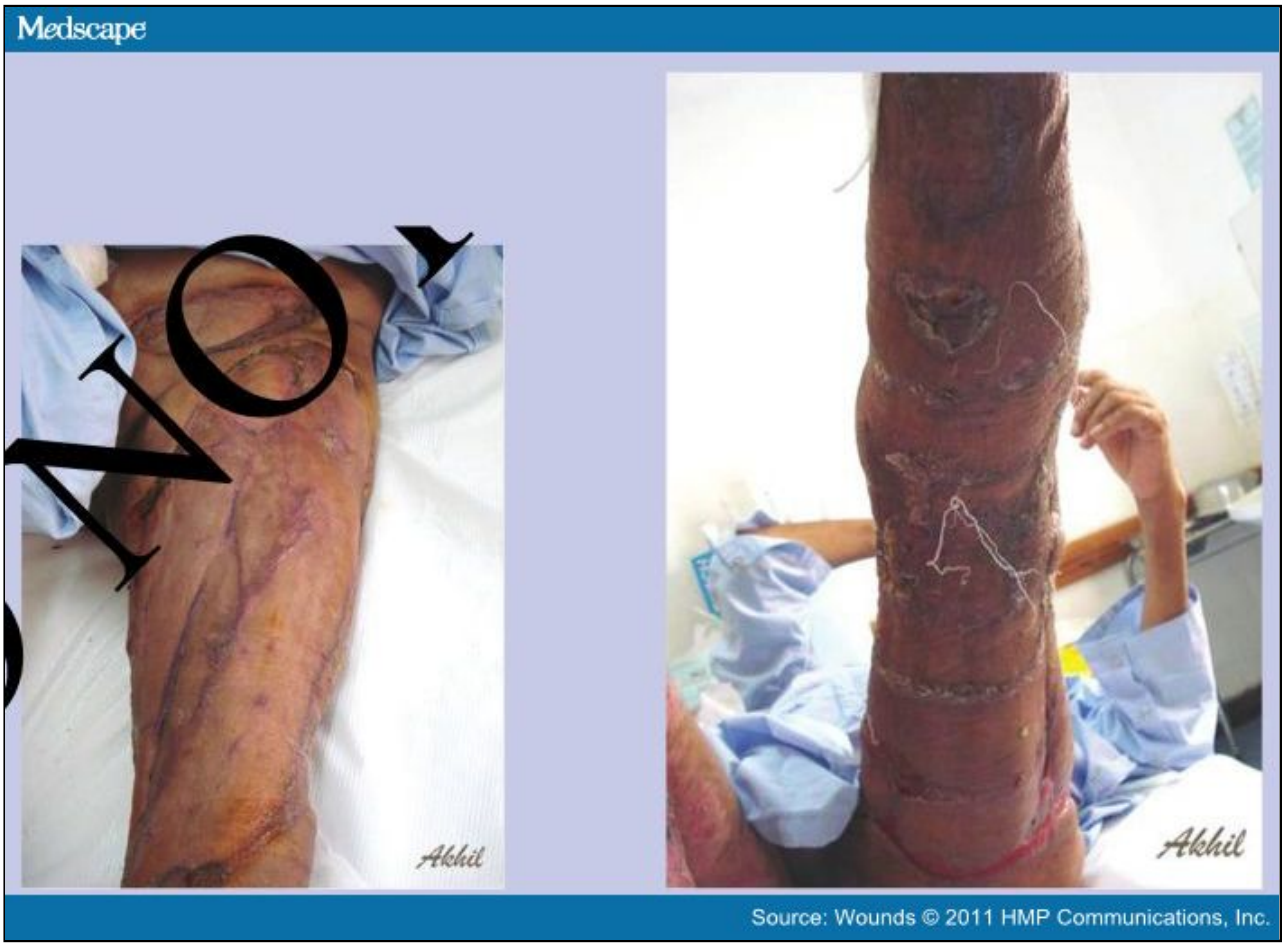


**Figure 4.** **a** Graft take was very good. **b** Healing was satisfactory.

## Discussion

Necrotizing fasciitis is a progressive and rapid necrotizing process characterized by widespread fascial necrosis sparing only the underlying muscle. Initially, the skin is intact, but it becomes gangrenous secondarily.[3,8,9] It may present with non-specific redness, swelling, and edema around the primary wound or an area of sepsis, but in other cases there may be an appearance of cellulitis in an area some distance from the primarily affected region. The presenting feature may be a reddish spot or erythema on the skin. Erythema may be present diffusely or locally, but in some patients, excruciating pain in the absence of any cutaneous findings is the only clue of infection. Within 24–48 hours, erythema changes to a very painful reddish-purple color, frequently with associated blisters and bullae; bullae can also develop in apparently normal skin.

The bullae are initially filled with clear fluid, but rapidly take on a blue or maroon color. Multiple identical patches may develop to produce a large area of gangrenous skin. Once the bullous stage is reached, there is already extensive soft tissue destruction.[7,14] General symptoms may include malaise, fever, sweating, chills, nausea, dizziness, profound weakness, and tachycardia. Hypotension may be present initially or develop over time. Although the aforementioned features can occur with cellulitis, the rapid progression, poor therapeutic response, necrosis, extensive local tenderness, tachycardia, high-temperature hypotension, and altered level of consciousness are highly suggestive of NF. If the condition is untreated, frank gangrene will progress very rapidly. The fascial involvement is much more extensive than that of the apparently viable skin. In addition, there are severe systemic disturbances including toxemia, dehydration, mental apathy, and confusion. In fulminating cases, multi-organ system failure will occur, frequently resulting in death if left untreated.[7,17]

In many cases, the patient has some underlying condition that reduces resistance to infection and predisposes the patient to NF, such as HIV infection, ischemic change, diabetes mellitus, steroid therapy, chemotherapy, alcoholism, obesity, poor socio-economic conditions, and malnutrition. Necrotizing fasciitis can also occur as a complication of chickenpox, especially in children.[17,18] Because of the rapid progression inherent in NF, it is important to recognize and treat NF as early as possible in order to reduce mortality and morbidity.[3,4,16] Diagnosis of NF is not difficult when the skin necrosis or bullae are present. Familiarity with NF may facilitate earlier diagnosis and initiation of appropriate therapy, but occasionally the clinical features are subtle until extensive necrosis has occurred.[10] The underlying affected skin is dusky or purple in color and difficult to differentiate from cellulitis. However, patients with NF complain of severe pain, usually out of proportion to the clinical appearance of the skin affected. Early confusion, toxic condition, and failure to respond to non-operative therapy are highly suggestive of a necrotizing infection. The presence of cutaneous necrosis, bullae, or crepitus strongly suggests a necrotizing infection, and urgent surgical exploration is warranted.[17,18] Laboratory testing and radiological and histological investigations may also help to confirm the diagnosis.

Laboratory testing showed acidosis, signs of DIC, TPC, creatinine phosphokinase, elevated creatinine and urea, ESR, hypocalcemia, hypoalbuminemia, leukocytosis with left shift, normochromic, and normocytic anemia. Blood culture may have a positive Gram stain if the tissue fluid from the wounds shows clusters of bacteria or if the wound swab culture shows the growth of organisms.[13,19] In our patient, the wound swab showed growth of *Pseudomonas aeruginosa*.

Radiological investigations may detect air within the tissue spaces, which is highly suggestive of NF.[20] However, CTs and MRIs seem to produce better quality images.[21–23]

Skin biopsy and histopathology are both useful in diagnosing NF. Common pathologic features are liquefactive necrotic tissues, pus cells, thrombosis of subcutaneous blood vessels, clusters of bacteria along the fascial planes, and an unimpressive infiltration of acute inflammatory cells. The rapid performance of frozen-section soft-tissue biopsy early in the evolution of a suspicious lesion may provide a definitive and life-saving diagnosis.[24,25] Our histopathology result revealed denuded epidermis, necrotic dermis and subcutaneous tissue, focal hemorrhage, perivascular inflammation, fibrin clot, and clumps of bacteria.

Most of the literature on NF consists of case reports and retrospective reviews. It is difficult to perform prospective, randomized, controlled trials because of the rarity of NF and the difficulty in suspecting and recognizing this disease. For these reasons, most of the studies are retrospective, quite small, and do not provide an independent, blind comparison with a gold standard diagnostic method. The gold standard of treatment in NF is early surgical debridement followed by intensive therapy with broad-spectrum antibacterial coverage. The best indication for surgical intervention is severe pain, fever, and elevated CPK with or without radiographic findings. The earlier the treatment can be started, the better the chance of survival. Early empiric antibiotic treatment could include ampicillin or ampicillin/sulbactum combined with either clindamycin or metronidazole. Once the culture and sensitivity results are obtained, the antibiotic regimen can be adjusted.[10,14,17]

Debridement beyond the visible margin of infection is necessary. Repeated debridement may be required and should be continued until all necrotic tissue is removed. Inspection under a general anesthetic is mandatory within the first 24 hours to detect any further extension of a newly discovered necrotic tissue. Fasciotomy should be performed in extremities with compromised vitality. Supportive care involves fluid resuscitation, cardiac monitoring, renal function, ABG, aggressive wound

care, and adequate nutritional supplement. Patients with NF are in a catabolic state and require increased caloric intake to combat infection. Nutritional support can be given orally or through nasogastric feeding with high protein diet and IV infusion of albumin. Prompt and aggressive nutritional support has been shown to lower the complication rates.[17,18]

The use of hyperbaric oxygen to treat necrotizing soft tissue infection is controversial. Several series of investigations suggested that hyperbaric oxygen therapy (HBOT) significantly reduced mortality in NF patients. Proponents of hyperbaric oxygen treatment claim that it makes the patient's condition less toxic and diminishes the amount of tissue requiring excision. HBOT works by increasing the $PO_2$ in tissue; thus, HBOT increases destruction of anaerobic bacteria, reduces tissue edema, stimulates fibroblast proliferation, increases collagen formation, reduces ischemia, enhances the action of antibiotics, stimulates angiogenesis, and promotes granulation tissue formation.[26,27]

Intravenous immunoglobulin (IVIG) has been shown to be effective in patients with streptococcal toxic shock syndrome. IVIG contains many antibodies that neutralize the exotoxin super antigen secreted by the streptococcus bacteria. IVIG also reduces T cells, which decreases tumor necrosis factor (TNF). While prospective trials on the use of IVIG for the treatment of NF are lacking, their use shows some evidence of benefit.[28,29] One study reported a significant increase in survival in the group of patients receiving IVIG.[30]

The next step in the management of NF is wound coverage. Aggressive debridement performed early in the management of NF often leaves a significant defect. Wound closure can be undertaken when systemic sepsis has been eliminated, all nonviable tissue has been removed, and bacterial control in the wound has been established. The most common technique used for wound closure is split skin grafting.

## Conclusion

Necrotizing fasciitis is a rapidly progressive, devastating infectious disease of the soft tissue, clinically characterized by the fulminant destruction of tissue, systemic signs of toxicity, and the increased rate of mortality. Diabetes mellitus, HIV infection, and alcoholism can predispose patients to NF. The disease appears as simple wound cellulitis, but early confusion, toxic condition, and failure to respond to non-operative treatment is highly suggestive of a necrotizing infection. Rapid progression and propensity for soft tissue destruction warrants early intervention to decrease mortality and morbidity. Prompt surgical debridement, broad-spectrum antimicrobial coverage, aggressive wound care, and hemodynamic and nutritional support are life saving.

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