Necrotizing Fasciitis in an Elderly Female with Diabetes Mellitus

J Sabu Philip, V P Fay

Abstract
Necrotizing fasciitis is a rapidly progressing, life threatening soft tissue infection more common in patients with less resistance to infection. Although early diagnosis is the cornerstone of management, emergency surgical management, early antibiotic treatment, and hemodynamic stabilization decrease morbidity and mortality. This paper discusses the pathology of necrotizing fasciitis and relates the diagnosis, wound treatment, and rehabilitation via a case study of an elderly female with a history of diabetes mellitus who presented to an emergency department. Wound care included the application of negative pressure wound therapy for preparing the wound for reconstructive surgery.

INTRODUCTION
Necrotizing fasciitis (NF) is a rare but life threatening soft tissue infection leading to extensive necrosis of fascia and subcutaneous tissue.1 Untreated NF can lead to sepsis and death by rapidly spreading necrosis in skin and subcutaneous fat.2 The diagnosis of necrotizing fasciitis is based on clinical presentation, the patient’s history, and physical examination. Better outcomes are demonstrated when the affected area involves only the patient’s upper extremities, as compared to more extensive involvement of the abdomen, perineal region, or lower extremities.3 Conventional wound care by wet to dry dressing for maintenance of moisture balance of the wound and mechanical debridement followed by negative pressure wound therapy (NPWT) demonstrates improved outcomes when managing extensive wounds after surgical debridement of devitalized tissue. Negative pressure wound therapy prepares the wound for surgical closure, promotes faster wound healing, and improves skin graft outcomes by providing a bolstering effect to reduce graft failure.4

CASE PRESENTATION
A 69 year-old Latin American female with a 16 year history of diabetes mellitus (DM) treated with oral medications presented to the emergency department (ED) with a 3 day history of fever and lower abdominal pain. She reported a lower abdominal wall blister with no history of trauma or injury to the site, subjective fever with diaphoresis, shortness of breath, nausea, and chills. On admission, the patient had a temperature of 100.5o Fahrenheit, a pulse rate of 112 beats per minute, a respiratory rate of 22 breaths per minute, and a blood pressure of 96/55 millimeters of mercury (mmHg). Examination of the abdomen and perineum revealed a large abscess that spanned from the umbilicus to the left thigh and vulva, an area approximately 25x32 centimeters (cm) in diameter. Bullae were noted at the lower abdominal wall and vulva. The area was disproportionately tender to palpation, edematous, and erythematous. No lymph nodes were palpable. The white blood cell count (WBC) showed 22 × 10³ per liter (L), with 88% neutrophils and 12% lymphocytes, hemoglobin (Hg) of 11 grams per deciliter (gm/dl) with a hematocrit of 32%, and a platelet count of 429×10³ /L. The blood sugar was 168 milligrams (mg)/dl on admission. The hemoglobin A1C was 6.6 %, and renal function was near normal with a serum creatinine of 1.2 mg/dl.

To aid in diagnosis, a risk score was validated using the Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score. A presumptive diagnosis was made for NF based on a risk assessment score of 7, given the patient’s C-reactive protein (CRP), an inflammatory marker, was 150mg/L. A LRINEC score of ≥6 raises the suspicion of NF, and a score of ≥8 is strongly predictive of the disease. The variables listed in Table 1 are used for diagnosing soft tissue infections.5
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Table 1
Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) Score.5

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>UNITS</th>
<th>SCORE</th>
</tr>
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<tbody>
<tr>
<td>C-reactive protein</td>
<td>mg/dL</td>
<td></td>
</tr>
<tr>
<td>White blood cell count (per mm²)</td>
<td>15-25</td>
<td>1 point</td>
</tr>
<tr>
<td>&lt; 11 mm²</td>
<td>2 points</td>
<td></td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>g/dL</td>
<td></td>
</tr>
<tr>
<td>Serum creatinine</td>
<td>mg/dL</td>
<td></td>
</tr>
<tr>
<td>Serum glucose</td>
<td>mg/dL</td>
<td></td>
</tr>
</tbody>
</table>

DISCUSSION

Diagnosis

Clinical features that differentiate NF from other soft tissue infections include fever, tachycardia, hypotension, tense edema outside the involved skin, disproportionate pain, blisters and bullae, crepitus, and subcutaneous gas.6 These features, along with gross evidence of widespread fascial necrosis by direct inspection (during surgical examination under anesthesia), excludes infective gangrene, solitary perianal abscesses, periurethal abscesses, and diabetic gangrene. Extensive necrosis of the superficial fascia in the absence of macrovascular occlusion is a hallmark of NF. Focal necrosis, microvascular changes, and leukocytosis in debrided tissue examination are also diagnostic indicators.7 Histopathological examination may reveal necrosis of the fascia, polymorphonuclear infiltrate, and edema of the dermis, subcutaneous fat, and superficial fascia.3 Although laboratory findings are generally nonspecific, a laboratory examination may show an increased WBC and positive blood cultures. Imaging studies, including soft tissue x-ray, computerized tomography (CT) scan, and magnetic resonance imagery (MRI) are helpful if gas is present in the tissue.5 Gas is highly specific but not very sensitive for NF, and imaging studies should not delay surgery if crepitus is present.6 Blood cultures are positive in greater than 60% of cases with Group A streptococcal NF. Bacteremia is usually polymicrobial.

Differential Diagnoses

In this case scenario, given the patient’s co-morbidities, history, and the physical features as well as the extent of wound area, there were many considerations for possible infecting organisms. Microbial considerations and their related specific physical impacts and findings are illustrated in Table 2.

Microbiologic Findings of Soft Tissue Infections

In soft tissue infections, a wide spectrum of organisms, as shown in Table 3, are commonly obtained in culture. In a majority of studies, approximately two-thirds of cases are polymicrobial and one-third, monomicrobial, with predominantly gram positive bacteria.6

Table 2
Differential Diagnoses of Necrotizing Fasciitis1

<table>
<thead>
<tr>
<th>POSSIBLE DIAGNOSIS</th>
<th>DIAGNOSTIC FEATURE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chloridial cellulitis</td>
<td>Usually caused by Clostridium perfringens and is usually associated with trauma</td>
</tr>
<tr>
<td>Necrotizing aspergillous cellulitis</td>
<td>Seen in diabetes with mixed aerobic and anaerobic organisms</td>
</tr>
<tr>
<td>Methylo erythromitotic gangrene</td>
<td>Rare and seen in post-operative patients</td>
</tr>
<tr>
<td>NF Type I</td>
<td>Seen in patients with peripheral vascular disease with aneurysmal lesions</td>
</tr>
<tr>
<td>NF Type II</td>
<td>Microbiologically caused by Streptococcus Group A (GAS) and Streptococcus pyogenes</td>
</tr>
<tr>
<td>Synergistic necrotizing fasciitis</td>
<td>Polymicrobial infection and is seen in leg ulcerations and is associated with EMF</td>
</tr>
<tr>
<td>Fournier’s Gangrene</td>
<td>Affects perineal area by putatives of native organisms (aerobic and anaerobic organisms) through gastrointestinal or genital sources</td>
</tr>
</tbody>
</table>

Table 3
Common Organisms Causing Necrotizing Fasciitis.8,9

<table>
<thead>
<tr>
<th>CLASSIFICATION</th>
<th>SPECIFIC ORGANISM</th>
</tr>
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<tbody>
<tr>
<td>Gram positive aerobic bacteria</td>
<td>Group A Beta-hemolytic streptococci, Group B streptococci, Enterococci, Coagulase negative staphylococci, Staphylococcus aureus, Facultative species, Staphylococcus epidermidis</td>
</tr>
<tr>
<td>Gram negative aerobic bacteria</td>
<td>Enterobacteriaceae, Pseudomonas aeruginosa, Proteus species, Bacteroides species</td>
</tr>
<tr>
<td>Anaerobic bacteria</td>
<td>Bacteroides species, Clostridium species, Peptostreptococcus species</td>
</tr>
<tr>
<td>Fung</td>
<td>Zygomycetes, Mucor, Aspergillus, Candida</td>
</tr>
<tr>
<td>Other</td>
<td>Yeast species</td>
</tr>
</tbody>
</table>

Pathophysiology

The etiology of NF is not fully understood. The disease occurs in patients with immunosuppression, diabetes, peripheral vascular disease, malignancy, and renal failure. Additionally, NF is commonly found in patients who are obese (moisture and sweat), have been prescribed steroids (immunosuppression), use intravenous drug (autoinjection of bacteria), or are over the age of 60 (poor immunity).1 Common pathologic features of NF include extensive tissue destruction, thrombosis of blood vessels, bacteria spreading...
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Necrosis provokes an inflammatory reaction in the surrounding tissue and is an irreversible process resulting in disruption of genetic material, plasma and organic cell membranes. In later stages, karyolysis (disruption of the cell nucleus) occurs, the nucleus shrinks, and karyorrhexis (rupture of the cell nucleus followed by fragmentation) occurs. After entering the human body, organisms secrete exotoxin A which stimulates production of cytokines and causes damage to the endothelial lining. This process leads to leakage of fluid into tissue, causing hypoxemia, diminished blood flow, and tissue death. Vasculitis and thrombosis occur in adjacent tissues leading to necrosis and nerve damage. If untreated, tissue necrosis progresses to gangrene within 4-5 days, followed by sloughing in the second week. Toxins enter into the blood stream within 24-96 hours, leading to sepsis and possible death. Other complications include disseminated intravascular coagulation (DIC), respiratory failure, and multisystem organ failure. Skin color changes from an initial redness to dusky blue, and initial complaints of pain change to numbness due to tissue and nerve death.

During infection, increased tissue catabolism increases the endogenous production of glucose. Polymicrobial infections resulting from hyperglycemia and micro-thrombosis of cutaneous arterioles are common. Hyperglycemia affects the phagocytosis, adherence, and bactericidal activities of phagocytes, causing detrimental effects on cellular immunity, and promotes the growth of microorganisms in the injured tissue. Hyperglycemia can lead to low immunity and high rate of infection due to inhibition of Glucose-6-phosphate dehydrogenase (G6PD) or diversion of nicotinamide adenine dinucleotide phosphate-oxidase (NADPH) in the polyol (sorbitol-aldose reductase) pathway. Diabetes prolongs the inflammatory response to bacterial stimulus through cytokine dysregulation.

Necrotizing Fasciitis Management

Broad Spectrum Antibiotics/Surgical Debridement

Presumptive antibiotic treatment should be initiated, and definitive treatment instituted after obtaining culture results. Initiation of antibiotic therapy within 1 hour of onset of septic shock results in better prognosis. Broad spectrum antibiotics with gram positive, gram negative and anaerobic bacteria specificity should be started early. Monotherapeutic agents include imipenem, meropenem, piperacillin, tazobactam, and tigecycline. Multidrug regimens (e.g., triple drug regimens, including penicillin, clindamycin, and a fluoroquinolone or an aminoglycoside for gram negative coverage) are indicated.

After starting intravenous antibiotics, surgical debridement is an immediate consideration. A surgical referral for debridement of the nonviable tissue should be done as soon as possible. Hemorrhage is inevitable due to extensive debridement or DIC, and the risk of hemorrhage mandates close monitoring of intra and postoperative hemoglobin. Throughout treatment, further surgical debridement, and blood transfusions may be needed. Broad spectrum antibiotic therapy is usually continued for 10-14 weeks or until there is no need for further debridement, and the patient is asymptomatic. A peripherally inserted central catheter (PICC) is beneficial for antibiotic therapy, and antibiotic levels should be monitored, if indicated. Reconstructive surgery is an option after eradicating the infection and preparing the wound for further surgery.

Negative Pressure Wound Therapy

Negative pressure wound therapy (NPWT) assists in preparing the wound for surgical closure by developing granulation tissue to cover the exposed tendon or bone. Application of NPWT by increasing blood flow to the wound bed stimulates granulation tissue formation and reduces edema that contributes to decreased tissue perfusion. Thus, the therapy contracts wounds so that less complex procedures (i.e., split thickness skin grafts) can be used instead of more complex procedures (i.e., free flaps). The therapy also provides a bolstering effect to improve graft survival, thereby reducing graft failure. Compared to conventional wound care, NPWT increases patient comfort, removes exudates, prevents surrounding skin maceration, and reduces frequency of dressing changes.

A NPWT machine and supplies is shown in Figure 1. Users should follow the company’s manual when applying vacuum assisted dressings and review guidelines published by the Food and Drug Administration (FDA) (http://www.fda.gov/safety/MedWatch/Safety Information/Safety Alerts for Human medical products/ucm190704.htm).
Use of NPWT is contraindicated for a wound with >25% necrotic tissue. Sharp or enzymatic debridement is performed as needed for complete removal of necrotic tissue prior to NPWT application to prevent infection and expedite the healing process. The use of hyperbaric oxygen along with antibiotics promotes tissue oxygenation and reduces edema. Administration of 95-100% of oxygen at pressure greater than 1.0 atmospheric absolute can cause an increase in partial pressure of oxygen in the blood, which promotes wound healing by tissue oxygenation and reduces edema by vasoconstriction. Formation of new epithelium and blood vessels causes faster wound healing.

Diabetes (Blood Glucose) Management

Diabetes is present in 32-66% of cases where NF has been definitely diagnosed. Diabetes can cause microvascular and macrovascular changes, thereby affecting the intracellular oxidative destruction of pathogens, neutrophil adhesion, chemotaxis, and cellular immunity. During the infection, the endogenous production of glucose increases, and hyperglycemia leads to growth of organisms in the injured tissue and decreases cellular immunity. Polymicrobial infections resulting from hyperglycemia and micro-thrombosis of cutaneous arterioles are common. Poor glucose control leads to the pathogenesis as well as poor outcome of NF. An individualized plan for blood glucose control to achieve an optimal hemoglobin A1C level should be instituted.

Pain Management

Moderate to severe pain is common in patients with NF because of the large area of soft tissue necrosis and subsequent surgical debridement. Because the process of dressing changes involves removing the dressing, cleaning the wound and reapplying a dressing, patients are more comfortable if pre-medicated for anticipatory pain prior to dressing changes. Factors causing wound pain (e.g., infection, colonization, trauma, inflammation, and maceration of the surrounding skin) should be controlled as much as possible. Adopting a holistic and patient-centered pain management approach assists in better pain management. In addition to providing analgesia with opioids, measures such as proper seating, positioning to avoid added pressure to the affected wound areas, and the use of adaptive equipment assist in pain control. Care should be taken in moistening and removing the dressing to avoid disruption of healthy granulation tissue.

Nutrition Consult and Management

Malnutrition is considered a major risk factor for complications and delayed recovery in hospitalized older adults and can result in higher morbidity, mortality, and health care expenses. A dietary consult and regular follow up aid in achieving better patient outcomes. Although laboratory tests, including serum albumin and pre-albumin (Transhyretin), are valuable in assessing and monitoring nutrition, these tests should not be used as the “gold standard” because other factors can affect a single measure. Sepsis and surgery increase metabolic needs, and therefore, calorie requirements double for patients with NF. Aggressive nutritional support improves the rate of wound healing. An increase in prealbumin from baseline denotes improved nutritional status and correlates with patient outcomes. In patients with acute inflammation, acute alcohol intoxication, and steroid use, albumin shows a more reliable and pre-existing nutritional status than prealbumin. Prealbumin is not a reliable indicator because the marker has a relatively short half-life of 2.5 days. CRP (an acute phase reactant) needs to be checked to evaluate the presence of inflammation. Nutritional supplements rich in protein should be included in the dietary management.

Minimizing Deconditioning

Functional limitations, pain, and restricted mobility due to deconditioning from hospitalization and the wound itself may challenge recovery from NF. Progressive rehabilitation done daily as tolerated promotes independence and mobility. Strategies to minimize deconditioning and enhance functional status include early mobilization, exercise and rehabilitation, pain control, nutritional supplementation, and minimally invasive surgery.

Candidiasis Control

Women with DM are prone to candidiasis colonization as
hyperglycemia suppresses immunity. This commonly associated finding leads to delayed wound healing in patients with diabetes. Vulvovaginal candidiasis is also common after treatment with broad spectrum antibiotics, and a viable option is to treat the surrounding areas of the wound with topical nystatin powder which controls the moisture rather than using antifungal creams.

Comprehensive Wound and Co-Morbidity Management in the Presented Case
Under general anesthesia, the case study patient underwent debridement of the lower abdominal wall, perineal area, and left posterior thigh. The necrosed layers of subcutaneous tissue with thrombosed blood vessels were removed, and the tissue was sent for gram stain and culture. In the intensive care unit (ICU), the patient was monitored for hemodynamic stability. Transient hypotension on admission was resolved with 3 liters of normal saline. Broad spectrum antibiotics (penicillin G, vancomycin, and clindamycin) were started and narrowed down to cefepime, metronidazole, and vancomycin according to the wound culture for Group D enterococcus. On the third day, the patient received further debridement of the necrotic tissue and fascia and was transfused with 3 units of blood. The patient’s hemoglobin of 5.9 gm% improved to 9 gm% post transfusion.

On the fifth day, the patient was extubated and transferred to a general care unit. The patient was hemodynamically stable, the WBC count trended down to normal range, and the blood sugars were normalized. Intravenous fentanyl was discontinued, and the patient was started on oral pain medications and oral nutrition. The patient was transferred to the skilled nursing facility on the fourteenth day for wound care and rehabilitation.

The wound was managed by conservative wet to dry dressing for the first week to promote a clean environment before transitioning to NPWT for 2 weeks. Negative pressure wound therapy with polymicrobial gauze was applied continuously at 100 mmHg to the lower abdominal wall, suprapubic, and left posterior thigh wound every Monday, Wednesday, and Friday. The exposed tendon on the inner thigh was protected with non-adherent dressings to prevent any injury. By the second week, a greenish drainage was noted and NPWT suspended. Dakin’s solution (1/4 strength) wet to dry dressings were applied for 5 days to treat the possible superficial pseudomonas colonization before switching back to NPWT. After the wounds contracted with 100% granulation tissue, the patient was transferred to the acute facility for a split thickness skin graft. The skin graft tissue was taken from the right thigh, and the donor site was medicated with bacitracin ointment; non-adherent dressings were changed every other day. Pictures of the wound after wound care are shown in Figure 2.

**Figure 2**
Photo A - Lower abdominal, vulvar wounds after wound care and Photo B - Left thigh wound after wound care

Along with wound therapy, the patient was treated for vulvar candidiasis with topical nystatin powder on the surrounding areas of the wound for 2 weeks. The patient had an indwelling Foley catheter to prevent wound contamination. To manage pain, the patient was pre-medicated with morphine sulfate 4 mg intramuscular (IM) prior to each dressing change. The patient was scheduled acetaminophen/hydrocodone every 6 hours and tramadol as needed for breakthrough pain. Nutritional supplements (Glytrol® 1 can orally twice daily between meals) and protein powder (Beneprotein® 1 scoop orally twice daily) were added to the treatment along with mirtazapine 7.5 mg by mouth daily to stimulate appetite. The patient’s prealbumin was monitored weekly to ensure her nutritional status, and her weight was monitored weekly.

Because the patient had diabetes, finger stick blood glucose was checked before meals and at bedtime. A diabetic diet and sliding scale insulin were continued for promoting glycemic control and wound healing. Metformin 1000 mg orally twice daily and glyburide (3 mg in the morning and 1.5mg in the evening) were administered. A low dose of lisinopril was started to prevent diabetic nephropathy due to microvascular complications. The patient underwent progressive rehabilitation and was able to walk with a rolling walker by the fourth week of inpatient rehabilitation stay. Home health nursing was arranged for continuation of wound care and rehabilitation at home.
Continuity of Care/Implications for Advanced Practice Nurses

Continuity of care is best achieved through a multidisciplinary approach to case management. Advanced practice nurses (APNs), who are often charged with the daily comprehensive care of patients, are in unique positions to lead and organize multidisciplinary teams. Unlike the rotational nature of medical/surgical residents in teaching hospitals, APNs are unit or team based. Thus, patient/family/APN provider relationships can be more consistently established. The APN organizes daily healthcare and expedites follow-up care. In this case scenario, an APN managed communications with the primary care physician about the patient’s care and coordinated medical/rehabilitation care and specialty follow up appointments.

Discharge instructions included directions for diabetes management, wound care, home exercises, fall prevention, and home safety as well as instructions to optimize medication compliance. The patient was advised on signs of infection, including redness, swelling, increased pain, fever, purulent drainage, or disruption of integrity of the skin graft. The patient was informed to call the primary care physician or the ED if signs of infection occurred. Home physical therapy was arranged for 3 times per week for 2 weeks to enhance strength, mobility, and promote independence for activities of daily living. The patient and the family were educated on wound care and home rehabilitation. Home health wound care was arranged for 3 times per week for 2 weeks to provide wound care and monitor wound healing as well as to provide family education.

CONCLUSION

Conclusion

Necrotizing fasciitis is a rare but potentially fatal condition, especially in elderly patients with diabetes. The etiology is not fully understood, but pre-existing conditions lead to susceptibility. Early diagnosis is primarily by clinical presentation and laboratory findings, including the use of adjunct diagnostic tests. Management focuses on early diagnosis, effective surgical debridement, administration of broad spectrum antibiotics, hemodynamic stabilization, and supportive care. The use of negative pressure wound therapy facilitates wound granulation tissue formation and wound contraction for surgical reconstruction. The APN’s role is vital to ensure care coordination within the interdisciplinary team for the management of this debilitating condition.

References

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Author Information

Jessy Sabu Philip, MSN, RN, GNP-BC, CCRN, CWCN, Gerontology Nurse Practitioner Doctoral Student
The University of Texas Health Science Center at Houston School of Nursing
Houston, Texas, USA

Vaunette P. Fay, PhD, RN, FNP-BC, GNP-BC Professor
The University of Texas Health Science Center at Houston School of Nursing
Houston, Texas, USA