Acute necrotizing fasciitis in Egyptian patients: A case series

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Abstract

Hyperacute soft tissue infection is an uncommon infectious entity, which mostly affects immunocompromised individuals, mainly diabetics and poses difficult diagnostic and therapeutic management decisions. This study addresses the presentation, evaluation and management of 37 diabetic patients with acute necrotizing fasciitis treated throughout the period between August 1993 and July 2006 by the main author. Extremities, trunk and perineum were the most commonly involved sites with an incidence of 35%, 30% and 27%, respectively. All patients presented with cellulitis, which was associated with oedema in 75.6% of cases, skin gangrene in 59% of cases and brown ecchymotic patches in 30% of cases. Skin vesicles, tenderness and crepitations were present in 13.5%, 11% and 11% of cases, respectively. Streptococci, Staphylococci and E. coli were the most commonly encountered organisms, which affected 70% of cases, either alone or in combination. Anaemia and hypoalbuminaemia were the most commonly encountered laboratory findings in 75.6% and 84% of cases, respectively. The mortality rate in the 37 patients included in this study was 43% (16 cases); in 11 of them the infection was located in the trunk and perineum. Once necrotizing fasciitis is suspected, exploration of the fascia is mandatory with pathological assessment of tissue specimens. Radical debridement of the affected area, maintenance of adequate nutritional support and systemic antibiotic therapy should be implemented at once in order to reduce mortality and insure safe recovery of patients.

1. Introduction

It is widely believed that patients with uncontrolled diabetes are not only susceptible to infection, but that also when infection does occur it is more severe. Certain types of organisms and certain sites of infection seem to be more common in diabetics such as: pulmonary tuberculosis, rhinocerebral mucormycosis, malignant otitis externa, emphysematous cholecystitis, renal papillary necrosis, non-clostridial gas gangrene, necrotizing cellulitis, vertebral osteomyelitis, vulvovaginal candidiasis, periodontitis and injection site abscess.1-4

Foot infections are the most common soft tissue infections in patients with diabetes. Among nonpedal soft tissue infections, necrotizing fasciitis is the most important. It is a rare, rapidly progressing infection affecting the superficial fascia and subcutaneous tissue, accompanied by severe systemic toxicity and multiorgan dysfunction.5 This hyperacute soft tissue infection has no pathognomonic signs. Patients may present with some evidence of cellulitis, vesicles, bullae, oedema, crepitus, erythema and fever. Patients may also complain of pain that seems out of proportion to the physical findings; as the infection progresses, their pain may decrease. No
single organism or combination of organisms is consistently responsible for necrotizing fasciitis.  

2. Materials and methods

This study represents a personal experience with the management of 37 cases of histopathologically confirmed acute necrotizing fasciitis treated throughout the period between August 1993 and July 2006. The clinical criteria, which raises the suspicion of acute necrotizing fasciitis include:

1. Immune compromised individuals (diabetics).
2. The presence of an inflammatory lesion in association with severe systemic toxicity.
3. Lack of clinical response to proper medical treatment for 48–72 h.
4. The presence of bullae away from the infection site.
5. The presence of skin gangrene.

Following history taking and physical examination patients were subjected to routine laboratory investigations, plain chest X-ray and cardiological evaluation when indicated. Following initial resuscitation, standard treatment after admission included cardiovascular stabilization and assessment of the extent of infection. Broad spectrum antibiotics were administered to cover gram positive cocci, gram negative enteric rods and anaerobic flora, usually in the form of a combination of Clindamycin 600 mg IV/6 h, third generation cephalosporins 1 g IV/12 h and/or aminoglycosides daily requirement over 250 cc saline over half an hour.

Patients were taken to the operating room for surgical exploration of the fascia in the affected site, which was performed under local anaesthesia. The classic operative features of serosanguineous discharge, undermining of the skin, sparing of the underlying muscle as well as dull, oedematous, grey necrotic or gangrenous fascia confirmed the diagnosis of necrotizing fasciitis (Figs. 1 and 2). Accordingly, a smear was sent for bacteriological evaluation and a full thickness skin biopsy was sent for histopathological evaluation (frozen section technique). Histologically, necrotizing fasciitis is characterized by obliterator endarteritis and thrombosis of the subcutaneous vessels; fascial necrosis, leukocytic infiltration with microabscess formation and absence of underlying muscle involvement.

Radical debridement was performed under general endotracheal anaesthesia and excised tissues were sent for histopathological evaluation. Multiple paraffin blocks were prepared from all excised material including the skin and/or muscle (if surgically excised); slides were prepared and stained with haematoxylin and eosin as well as Masson trichrome stains.

Critical support was required for most of the patients and was routinely comprehensive and aggressive. Prolonged mechanical ventilation, invasive monitoring and inotropic support frequently were necessary for cardiopulmonary failure. Repeated debridement was performed according to the wound status, which was dressed twice daily with saline, hydrogen peroxide, betadine and topical crystalline penicillin 5–10 million units. Following the improvement of the general condition and wound cleansing, patients were subjected to wound secondary sutures or coverage of the raw area with a split skin graft. In one case, bilateral inguinoscrotal flaps were performed to cover the exposed testes in a patient with perineal necrotizing fasciitis. In another case a rectus abdominus myocutaneous flap was used to cover the exposed femoral artery following radical debridement of the thigh.

3. Results

3.1. Location (Table 1)

Out of the 37 patients included in the study there were 27 men and 10 women (2.7:1). Their age ranged from 15 to 85 years with a mean of 52.5 ± 9.5 years. The infection involved the upper limb in one case (3%), the head and neck in three cases (8%), the lower limb in 12 cases (32%), the perineum and scrotum in 10 cases (27%) and the abdominal wall in 11 cases (30%) as shown in the table1 and Figs. 3–7.
3.2 Bacterial aetiology (Table 2)

The haemolytic streptococcus was the major organism cultured from the wound in 10 cases (27%). Pathogenic staphylococcus was the predominant organism in another eight cases (21.6%), 11 of these 18 patients had both organisms present in significant quantity. Eight cases (21.6%) had E. coli as the major offending organism; this mainly was encountered in the perineum and abdominal lesions. The remaining 11 cases (29.8%) had proteus organism isolated in three cases (8%), enterobacter in three cases (8%), diphtheroid in one case (3%) and pseudomonous aurigenosum in four cases (10.8%).

3.3 Predisposing factors (Table 3)

Necrotizing fasciitis developed spontaneously in 11 cases (30%), following a minor trauma such as abrasions, cuts and bruises in seven cases (19%), after dental extraction in two cases (5%), and an insect bite in one case (2.7%). It followed diabetic foot infection in five cases (13.5%), has unknown predisposing factors in seven cases (19%) and it followed surgical procedures in four cases (10.8%); one case followed the insertion of a subclavian central venous line in a critically ill patient in the ICU, another one followed an aortic valve replacement, one followed a coronary artery bypass surgery and the infection involved the lower limb at the site of retrieval of the saphenous vein, while the last case followed an abdominal exploration for a case of neglected strangulated recurrent huge right oblique inguinal hernia.

3.4 Associated illness

All the 37 cases included in this study suffered diabetes mellitus alone or in association with other diseases (25 cases). Eleven cases had hypertension, three had associated malignancies (pancreatic cancer, leukaemia and osteosarcoma), five had ischaemic heart diseases, five had liver cirrhosis, and one had cerebral palsy.

3.5 Diagnosis

Necrotizing fasciitis occurred in all ages from 15 to 85 years, mostly in patients over 40 years of age. The signs and symptoms of necrotizing fasciitis varied. Cellulitis was present in all cases. Eleven patients (30%) had brown ecchymotic skin discolouration and 16 (59%) had cutaneous gangrene. The number of patients with skin gangrene was large due to...
misdiagnosis by the primary treating physician or late presentation of cases.

Skin anaesthesia was present in eight cases (21.6%), although it was not tested in many patients. Skin vesicles were less common, being present only in five cases (13.5%). Mild to moderate oedema was present in 28 patients (75.6%). This along with calf tenderness simulated deep vein thrombosis in four cases (11%); two of them were given anticoagulant drugs and managed conservatively because the true condition was not diagnosed until patients were referred for surgical consultation.

Crepitation has been thought to be pathognomonic of clostridial infection. However, it is known that other organisms can create crepitation as does E. coli infection in diabetics. Four patients (11%) had subcutaneous crepitation, and in one patient subcutaneous gas was demonstrated on CT scan (Fig. 8), yet smear and cultures failed to grow clostridial organisms. The average temperature was 38.5 °C with a range of 37–40.5 °C and it was usually of a spiking or septic pattern.

3.6. Laboratory data

Haemoglobin levels were monitored because the red cell mass was frequently diminished by thrombosis, ecchymoses, sequestration by the reticuloendothelial system and haemolysis. Production of red cells by the bone marrow was often depressed by infection and toxaemia in these patients. In 28 cases (75.6%), the haemoglobin level was below 10 g %. Serum calcium level is decreased in the acute phase. Presumably fat splits into fatty acids by bacterial lipase and the ionic calcium combines with fatty acids to form insoluble soaps in the subcutaneous tissues. Most patients showed a mild drop in serum calcium but no tetany was observed. Deficiencies were

<table>
<thead>
<tr>
<th>Organism</th>
<th>Number of cases</th>
</tr>
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<tbody>
<tr>
<td>Haemolytic streptococci</td>
<td>10 (27%)</td>
</tr>
<tr>
<td>Staphylococcus epidermis</td>
<td>8 (21.6%)</td>
</tr>
<tr>
<td>E. coli</td>
<td>8 (21.6%)</td>
</tr>
<tr>
<td>Pseudomonous Aurigenosum</td>
<td>4 (10.8%)</td>
</tr>
<tr>
<td>Enterobacter</td>
<td>3 (8%)</td>
</tr>
<tr>
<td>Proteus</td>
<td>3 (8%)</td>
</tr>
<tr>
<td>Diphtheroids</td>
<td>1 (3%)</td>
</tr>
</tbody>
</table>
corrected with intravenous calcium gluconate. White cell count, serum electrolytes, blood urea nitrogen, and other laboratory studies showed non-specific changes of other serious acute infections. In 31 cases (84%) serum albumin level was below 3 g/dl, this is probably due to associated malnutrition, compromised liver functions due to prevalence of bilharziasis and hepatitis C and the effect of bacterial toxins. Hypoalbuminaemia was considered as an indirect indicator of immune suppression, and mandated intravenous albumin therapy in order to maintain homeostasis.

3.7. Management

Once the diagnosis of necrotizing fasciitis was suspected aerobic and anaerobic wound cultures were obtained. The patient was given a combination antimicrobial chemotherapy as mentioned earlier. Correction of fluids, electrolytes and red cell mass deficiencies was carried out and the fever treated with antipyretics and cold foment. After resuscitation and under general endotracheal anaesthesia, incisions were made down to the superficial fascia for inspection. Once the diagnosis was confirmed, multiple linear incisions or skin excision were made over the affected area and carried beyond the fascial extension as determined by finger dissection in that plane.

After the infection was controlled and granulation tissue covered the wound, the sides of the wound were loosely approximated. This reduced the healing area and the number of skin grafts required to close the defect. The 21 patients (57%) who survived were subjected to amputation in five cases (one above elbow and four above knee amputations), split skin grafts in seven cases, secondary sutures in four cases, bilateral inguinoscrotal flaps to cover the exposed testes in a patient with perineal necrotizing fasciitis, Rectus abdominus myocutaneous flap for the coverage of the exposed femoral artery following extensive debridement of the upper part of the right thigh in a female patient who developed necrotizing fasciitis of the right lower limb at the site of saphenous vein retrieval for coronary bypass surgery, and in the remaining three cases the raw area was left to heal by secondary intention.

3.8. Morbidity and mortality

The average period of hospitalization was 3 weeks. The shortest period was in an elderly patient who presented with septic shock and expired soon after admission. The shortest period of hospitalization for a survivor was 8 days and the longest period was 65 days. The mortality rate in the 37 patients was 43% (16 cases). Out of the 16 cases who died 2/3 involved the neck, 3/13 involved the extremities and 11/21 involved the trunk and perineum. Several factors were responsible for mortality in this study including: Diabetes mellitus, associated uncontrolled hypertension, associated ischaemic heart disease, liver cirrhosis, chest infection and multiple organs dysfunction.

The most important factor in survival was related to the rapidity of diagnosis and institution of therapy. The average time from the onset of the disease to the diagnosis and institution of therapy was 2 weeks. However, this period averaged only 5 days in survivors as compared to 2 weeks in those who died ($p = 0.04$, chi-square test).

4. Discussion

Necrotizing fasciitis was first mentioned by Hippocrates around the fifth century AD as a complication of erysipelas. Joseph Jones in 1881, provided one of the earliest description of this clinical entity and named it hospital gangrene. Since then the disease was named, renamed and even misnamed necrotizing erysipelas, haemolytic streptococcal gangrene, suppurative fasciitis, acute dermal gangrene, phagedena and Fournier’s gangrene. Later on, the first accurate detailed description of the condition was made by Meleney in 1924 following a study of 20 patients in China. No additional progress was reported until 1952, when Wilson reported the largest series of cases to date and recommended that all previous names be dropped and the condition be referred to as acute necrotizing fasciitis, for he observed that cutaneous gangrene was not invariably present, but fascial necrosis was a constant feature of the syndrome.

Necrotizing fasciitis occurs at any age with a mean age variation from 32 to 57 years. In this study the mean age was 52 years and men were affected more than women as reported in other series. The reason for this difference cannot be explained. The majority of patients who developed necrotizing fasciitis have pre-existing conditions that render them susceptible to infection. The common factor appears to be an immunosuppressive effect resulting from advanced age, diabetes mellitus, acute or chronic renal failure, local effects such as peripheral vascular disease or lymphoedema that predisposes to local cellulitis. A number of other causes

**Fig. 8 – Abdominal CT scan showing the presence of gas underneath the skin and spreading through the layers of the anterior abdominal wall.**

**Table 3 – Predisposing factors for acute necrotizing fasciitis in this study**

<table>
<thead>
<tr>
<th>Predisposing factors</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous</td>
<td>11 (30%)</td>
</tr>
<tr>
<td>Minor trauma</td>
<td>7 (19%)</td>
</tr>
<tr>
<td>Unknown aetiology</td>
<td>7 (19%)</td>
</tr>
<tr>
<td>Post-surgical</td>
<td>4 (10.8%)</td>
</tr>
<tr>
<td>Diabetic foot infection</td>
<td>5 (13.5%)</td>
</tr>
<tr>
<td>Dental extraction</td>
<td>2 (5%)</td>
</tr>
<tr>
<td>Insect bite</td>
<td>1 (2.7%)</td>
</tr>
</tbody>
</table>

of necrotizing soft tissue infections have been implicated such as intravenous drug abuse, previous trauma, after operations and insect or animal bites; however, many adult cases are idiopathic.16

Distinguishing necrotizing fasciitis from other less severe infections is difficult but crucial, since necrotizing fasciitis is a surgical emergency. A majority of patients present with an erythematous, tender, swollen area resembling cellulitis with disproportionately severe pain at the site of involvement without enlargement of the draining lymph nodes. Other less common presenting complaints include fever, chills, weakness, confusion and rash. As the infection progresses, the skin characteristically becomes more erythematous, painful and swollen with indistinct borders. The skin develops a violaceous hue, may become necrotic with bullae formation and eventually appears haemorrhagic and gangrenous. There may be involvement of more than one area, separated by islands of normal skin.11,13,16

In this study, all included patients presented with cellulitis. Oedema was present in 28 patients (75.6%), brown ecchymotic patches in 11 cases (30%), skin gangrene in 16 cases (59%), skin vesicles in five cases (13.5%), tenderness in four cases (11%) and crepitations in four cases (11%). The high incidence of skin gangrene was presumably due to delay in presentation from the patient side and delay in diagnosis and institution of therapy from the physician side, due to the difficulty in diagnosis and the lack of awareness of the condition and the proper way of setting up an early diagnosis. The early diagnosis of necrotizing fasciitis with a subsequent operative debridement has been shown to improve survival.17 Delayed diagnosis is frequently seen because early in the evolution of this disease, it is often clinically indistinguishable from other soft tissue infections such as cellulitis and erysipelas.18 The Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score was developed with the hope that it may yield diagnostic clues of the presence of necrotizing soft tissue infection, even early in the evolution of the disease when clinical findings were non-diagnostic.19 This score includes: C-reactive protein (score 4), white cell count, haemoglobin, serum sodium, serum creatinine levels (score 2 for each) and blood sugar level (score 1), with a total score of 13. In a retrospective study, the cut-off score level of 6/13 was considered highly indicative of necrotizing fasciitis with a 92% positive predictive value and a 96% negative predictive value.20 A prospective study investigated the use of tissue oxygen monitoring with near-infrared spectroscopy for the diagnosis of necrotizing fasciitis and reported, at a cut-off tissue oxygen saturation of less than 70% a sensitivity of 100% and a specificity of 97%. The LRINEC score was applied on the cases included in this study and was found to have a positive predictive value of 40% and a negative predictive value of 95%, they concluded when clinical findings were non-diagnostic.19 This score may be useful to classify them as monomicrobial infection caused by streptococci (10%) or polymicrobial infections (90%) caused by facultative gram negative bacilli such as E. coli, K. pneumoniae and strict anaerobes such as Bacteroides fragilis or clostridium species.25

Patients expected of having necrotizing fasciitis should be started empirically on broad spectrum antibiotics covering the most commonly encountered pathogens. The most commonly advocated antibiotic regimen includes Ampicillin/ Penicillin, Gentamicin and anaerobic coverage with either Metronidazole or Clindamycin.12,14,16 In this study, we used third generation Cephalosporins, Aminoglycosides and Clindamycin. There is experimental evidence suggesting that Clindamycin may be superior to Penicillin in overwhelming streptococcal infections due to an inoculum effect of large numbers of slower growing organisms with decreased expression of certain Penicillin-binding proteins. Clindamycin is not subject to such an effect as it works by inhibiting protein synthesis; moreover, it suppresses the production of certain bacterial toxins.26 Subsequent antibiotic management is guided by the sensitivities of the organisms identified from intraoperative cultures, and should be continued until the infection is under control and for at least 48 h after the temperature and white cell count have returned to normal.

Radiographic evaluation has been used primarily for patients in whom the diagnosis was doubtful. Plain films of the involved area may show evidence of soft tissue air. CT scan and MRI have been employed in equivocal cases and have sometimes been helpful in defining the presence and extent of infection.23 It cannot be overemphasized, however, that these radiological studies are only adjuncts in the evaluation of patients with potential necrotizing fasciitis and should not be relied upon to exclude the diagnosis, which is primarily a clinical one. Most important, the extent of debridement is determined by physical findings at the time of surgery and not by CT findings.

Majeski and Majeski in 1997 reported that the only reasonable approach to the diagnosis is a bedside incisional biopsy down to the fascial level and immediate frozen section, culture and gram stain.24 Although necrotizing fasciitis can occur anywhere on the body, it is more common in certain locations. Extremities, trunk and perineum are the most commonly involved sites in this study with an incidence of 35%, 30% and 27%, respectively, this in comparison to 36–55%, 18–64% and up to 36% of cases, respectively, in other published series.12–16

Necrotizing fasciitis has been classified as type I (infection caused by a combination of anaerobic and one or more facultative aerobic organisms) or type II (caused by group A streptococci, with or without staphylococci). It is clinically more useful to classify them as monomicrobial infection caused by streptococci (10%) or polymicrobial infections (90%) caused by facultative gram negative bacilli such as E. coli, K. pneumoniae and strict anaerobes such as Bacteroides fragilis or clostridium species.25

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Once the diagnosis of necrotizing fasciitis is made, treatment should be instituted promptly. The patient should be brought to the operating room without unnecessary delay and undergo aggressive and extensive debridement. The skin, soft tissue and muscle should be debrided until there is no further evidence of infected tissue, based solely on the findings at surgery. The first operative debridement is the most important one for the survival of the patient. It is preferable to remove more tissues than necessary than to leave any actively infected or necrotic tissues. The patient should then
be returned to the operating theatre when necessary to remove any desiccated tissue and to confirm that there has been no extension of the infectious process. Once the infection is controlled, daily dressing can be done at the bedside with sedation followed by secondary suturing of the wounds with or without split skin grafts to cover the exposed soft tissues. Recently, the use of a Vacuum-assisted Wound Closing (VAC) device was found to be effective in managing non-healing limb wounds following debridement for patients suffering from acute necrotizing fasciitis. Despite being costly, it has a much lower morbidity when compared to the conventional wound dressing technique.27

The role of amputation in controlling necrotizing fasciitis is controversial. If infection can only be eradicated by amputation, it should be done promptly and without hesitation. Hyperbaric oxygenation has been suggested as a complimentary method of treatment based on the fact that once tissue oxygen tension is kept high, the end result would be increased leukocyte phagocytes on the edge of the wound. Many studies have questioned the efficacy of this treatment in decreasing morbidity and mortality in necrotizing fasciitis.28 29 Moreover, few institutions have facilities for hyperbaric treatment and patients are often too ill to be transported there for treatment.

The reported mortality rate for necrotizing fasciitis varies from 6% to 69%.30 32 In this study the mortality rate was 43%; this mostly was due to the delayed presentation of cases as evidenced by the high incidence of skin gangrene (59%). Death is usually due to sepsis, respiratory failure, kidney failure or multiple organs dysfunction. Lesions of the extremities have a better prognosis than those of the trunk and neck probably because definitive and more complete debridement is accomplished with less difficulty on the limbs.

In conclusion, necrotizing fasciitis is an uncommon infection that often presents for medical attention late in its course. The diagnosis is often missed at the initial presentation, allowing further progression of the infectious process. Patients most commonly present with pain at a soft tissue site, with erythema and tenderness. Once the diagnosis has been made, the patient is stabilized and taken to the operating room for debridement. Surgical debridement should be performed daily until the acute infection has been controlled. Outcomes are based on the promptness of diagnosis, surgical treatment and the management of postoperative complications.

Conflict of interest
None.

Funding
None.

Ethical approval
This study qualified for expedited review.

REFERENCES


