

Report

Staging of necrotizing fasciitis based on the evolving cutaneous features

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Abstract

Background Necrotizing fasciitis is a severe soft-tissue infection characterized by a fulminant course and high mortality. Early recognition is difficult as the disease is often clinically indistinguishable from cellulitis and other soft-tissue infections early in its evolution. Our aim was to study the manifestations of the cutaneous signs of necrotizing fasciitis as the disease evolves.

Methods This was a retrospective study on patients with necrotizing fasciitis at a single institution. Their charts were reviewed to document the daily cutaneous changes from the time of presentation (day 0) through to day 4 from presentation.

Results Twenty-two patients were identified. At initial assessment (day 0), almost all patients presented with erythema, tenderness, warm skin, and swelling. Blistering occurred in 41% of patients at presentation whereas late signs such as skin crepitus, necrosis, and anesthesia were infrequently seen (0–5%). As time elapsed, more patients had blistering (77% had blisters at day 4) and eventually the late signs of necrotizing fasciitis characterized by skin crepitus, necrosis, and anesthesia (9–36%) were seen. A clinical staging system was developed based on our observations. Stage migration from early to late stage necrotizing fasciitis was evident with majority of patients in stage 1 at day 0 (59%), whereas by day 4, majority had developed into stage 3 (68%).

Conclusion This study has demonstrated the continuum of cutaneous manifestations as necrotizing fasciitis evolves. This will help in the early recognition and intervention of this devastating condition.

Introduction

Necrotizing fasciitis is a life-threatening infection affecting the superficial fascia and subcutaneous tissue.^{1–3} Despite better understanding of the pathophysiology of this devastating infection, mortality remains high. This can in part be attributed to delayed recognition and operative debridement.^{1–10} Although many studies have clearly demonstrated that early operative debridement reduces mortality, early recognition is difficult as nascent necrotizing fasciitis often appears deceptively benign and lack specific diagnostic clues.^{1–7} As the disease evolves, cutaneous features manifest progressively. However, detailed description of the continuum of dermatologic manifestations of necrotizing fasciitis as the disease evolves from early to late stages is currently lacking. We aim to systematically document these progressive manifestations of cutaneous signs of necrotizing fasciitis as necrotizing fasciitis progresses from early through to late stages. This will enable early recognition, better define disease progression, and heighten awareness during serial evaluation of all soft-tissue infections.

Methods and Materials

A retrospective review was performed on the medical records of all patients treated at one institution (Changi General Hospital) for necrotizing fasciitis between January 1997 and August 2002. Patients were identified through a computer-generated search through the Medical Records Department for all patients diagnosed with necrotizing fasciitis. Eighty-nine consecutive records were found. Patients were taken care of by teams consisting dermatologists, internists, plastic, and orthopedic surgeons. The following characteristics at operative exploration were used for definitive diagnosis: the presence of greyish necrotic fascia, demonstration of a lack of resistance of normally adherent muscular fascia to blunt dissection, lack of bleeding of the fascia during dissection, and the presence of foul smelling “dish water” pus. Histopathologic tissue examination was used to confirm the diagnosis when available.^{11,12}

Of these 89 cases, only those with a period between admission and first surgical debridement of more than 96 h were selected for this study. Time of admission was defined as time at which the patients registered at the emergency department and time of

operative debridement was defined as the start time noted in the operative notes. These were patients in whom the diagnoses of necrotizing fasciitis were initially missed. They were admitted and treated as for cellulitis or erysipelas. This method of patient selection was necessary in order to study the progressive manifestation of cutaneous signs as the disease evolves from early through to late stages. Patients who presented in late stages of the disease would pose little diagnostic difficulty and were operated on immediately after presentation. These cases were therefore excluded.

Using our method of selection, 22 patients were identified. Their charts were retrospectively reviewed and the following were noted: documented clinical signs from the time of initial assessment and subsequently every 24 hours until the time of operative debridement. Features noted were: erythema, tenderness to palpation, swelling, calor (warm skin), blisters or bullae formation (serous or hemorrhagic), skin fluctuance, induration, anesthesia, crepitus, and necrosis (Figs 1–3). Photographic records were also reviewed when available.

Results

The study was composed of 15 men and 7 women. The mean age was 59 years (range of 28–83). Majority of infections occurred in the lower limbs (17 [77%] patients). Other sites included the upper limbs (2 [9%] patients), gluteal region (2 [9%] patients), and groin (1 [5%] patients). Majority of patients (19 [86%] patients) had at least one underlying comorbidity that predisposed them to necrotizing soft-tissue infections such as diabetes mellitus, immunosuppression, and chronic alcoholic liver disease. Only three patients (14%) had no associated predisposing factors for developing necrotizing fasciitis. The patients had been experiencing pain over the affected site for a mean duration of 2.8 days prior to admission (range 1–9 days). Table 1 gives a summary of patients' comorbidities and medication history.

The diagnosis of necrotizing fasciitis was initially missed in all 22 patients. All patients were treated as cellulitis and were given intravenous antimicrobials. The diagnosis of necrotizing fasciitis was made when the infection progressed despite antimicrobial therapy with the development of sepsis, ascending infection, and progressive cutaneous manifestations. The mean time from admission to operative debridement was 137 h (range 96–312 h, SD 79 h). This allowed for serial evaluation of the cutaneous changes of necrotizing fasciitis as the infection progressed.

Table 2 summarizes the cutaneous findings of our cohort of 22 patients at 0, 1, 2, 3, and 4 days, respectively (denoted by D₀, D₁, D₂, D₃, and D₄). Based on these observations, we propose a clinical staging of necrotizing fasciitis (Table 3). Table 4 shows the daily clinical stages of patients demonstrating stage migration toward more advanced disease as the infection evolves. At initial assessment (D₀), almost all



Figure 1 Early necrotizing fasciitis (stage 1) characterized by exquisite tenderness beyond the apparent margin of infection, erythema, swelling, and calor of the skin



Figure 2 Blister or bulla formation, usually filled with serous fluid initially (stage 2). Eventually blisters coalesced and bled resulting in a hemorrhagic bulla

patients presented with a combination of erythema, tenderness, calor, and swelling (86–100%) (Fig. 1). Blistering occurred in 41% of patients whereas the so-called hard signs of necrotizing soft-tissue infections such as skin crepitus, necrosis, and



Figure 3 Late necrotizing fasciitis with skin necrosis and crepitus (stage 3)

Table 1 Summary of the patients' gender, comorbidities, and medication history

	No. of patients (percentage)
Gender	
Male	15 (68)
Female	7 (32)
Comorbidities	
Diabetes mellitus	14 (64)
Peripheral vascular disease	4 (18)
Cancer	2 (9)
Chronic liver disease	1 (5)
No comorbidities	3 (14)
Drugs	
Long-term steroids	1 (5)
Nonsteroidal anti-inflammatory drugs (NSAIDs)	1 (5)

anesthesia were seen infrequently (0–5%). As the infection progressed, blisters progressively manifested in more patients (77% had blisters at D4) (Fig. 2). Majority of these patients went on to develop late signs of necrotizing fasciitis characterized by skin crepitus, necrosis, and anesthesia (9–36%). At D4, 15 (68%) of our cohort of 22 patients developed stage 3

Table 3 Clinical stages of necrotizing fasciitis. Cutaneous manifestations of necrotizing fasciitis as the disease progresses through stages 1, 2, and 3 (early, intermediate, and late stages). Skin areas with the most advanced changes should be taken as the clinical stage

Clinical stages of necrotizing fasciitis	Stage 1 (early)	Stage 2 (intermediate)	Stage 3 (late)
Clinical features	Tenderness to palpation (extending beyond the apparent area of skin involvement) Erythema Swelling Calor (warm skin)	Blister or bullae formation (serous fluid)	Crepitus Skin anesthesia Skin necrosis with dusky discoloration

Table 2 Documentation of the number of patients manifesting the cutaneous signs of necrotizing fasciitis monitored daily from the time of admission (D0) for 4 days

Cutaneous signs	D0	D1	D2	D3	D4
Tenderness	21	22	22	22	22
Erythema	21	22	22	22	22
Swelling	19	20	22	22	22
Rubor	22	22	22	22	22
Blisters	9	11	11	14	17
Crepitus	0	0	1	1	2
Skin necrosis	1	3	3	5	8
Skin anesthesia	0	0	0	2	5

Table 4 The number and percentage (in parentheses) of patients with stages 1, 2, and 3 cutaneous features noted at D0, D1, D2, D3, and D4, respectively. As time elapsed, more patients progressed from stages 1–2 to 3. Stage migration toward more advanced disease was noted with majority being in stage 1 at D0 (59%) to majority being in stage 3 at D4 (68%)

Clinical stage	Assessment of clinical stage of necrotizing fasciitis at time intervals after admission				
	D0	D1	D2	D3	D4
Stage 1	13 (59)	11 (50)	10 (45)	3 (14)	2 (9)
Stage 2	8 (36)	8 (36)	8 (36)	11 (50)	5 (23)
Stage 3	1 (5)	3 (14)	4 (18)	8 (36)	15 (68)

signs of necrotizing fasciitis, i.e., skin crepitus, necrosis, or anesthesia (Fig. 3). Thirteen of these 15 patients (87%) showed a continuous progression from stages 1–2 to 3. Blistering (heralding the onset of stage 2 necrotizing fasciitis) manifested a mean 37 h (range 24–72 h, SD 19 h) prior to the manifestation of stage 3 signs.

Discussion

As demonstrated in our study, the diagnostic signs that physicians have come to associate with necrotizing fasciitis,

such as crepitus, skin necrosis, and hemorrhagic bullae, occur late in the evolution of the disease. Although these signs are pathognomonic of necrotizing fasciitis, it is important that one is aware that its absence does not exclude the disease. As we have shown, considerable time elapsed before these signs are apparent (in stage 3 necrotizing fasciitis). In necrotizing fasciitis, the primary site of pathology is in the deep fascia. Skin manifestations are secondary changes resulting from progressive ischemia and therefore do not accurately reflect the extensiveness of the underlying infection. Early in the evolution of necrotizing fasciitis (stage 1 necrotizing fasciitis), the disease may be clinically indistinguishable from other soft-tissue infections such as cellulitis and erysipelas presenting with only pain, tenderness, swelling, and calor.¹⁻⁷ Blisters or bulla formation is an important diagnostic clue of necrotizing fasciitis.^{2,6} When present, it signals the onset of critical skin ischemia (stage 2 necrotizing fasciitis). In necrotizing fasciitis, blisters are caused by ischemia-induced necrosis as the perforators coursing through the fascia to supply the skin are progressively thrombosed by the invading organisms. Blistering or bullae formation is seldom seen in erysipelas or cellulitis and should raise the suspicion of necrotizing soft-tissue infection.^{7,8} The late stage (stage 3 necrotizing fasciitis) signals the onset of tissue necrosis and is characterized by the so called hard signs of necrotizing soft-tissue infection such as hemorrhagic bullae, skin anesthesia, and frank skin gangrene.^{1,2} Commonly, the skin changes are heterogenous and the skin area with the most advanced skin changes should be taken as the clinical stage.

Although early necrotizing fasciitis (stage 1) may be clinically indistinguishable from other soft-tissue infections such as erysipelas and cellulitis, some cutaneous features are helpful diagnostic clues. First, in necrotizing fasciitis, margins of tissue involvement are often poorly defined and indistinct. This is in contrast to more superficial soft tissue infections such as erysipelas. Second, tenderness extending beyond the apparent area of involvement is a further diagnostic clue.^{2,5,6} The primary site of pathology in necrotizing fasciitis is in the deep fascia and spread of infection along this plane is usually well ahead of cutaneous changes.^{11,12} Bacteria proliferate within the superficial fascia and elaborate enzymes and toxins that enable the organisms to spread through the fascia. Tenderness over apparently normal skin is a clue of this. In infections such as cellulitis, tenderness is usually confined to erythematous areas as these are more superficial infections. Third, pain is severe over the affected site, classically described as being out of proportion to physical findings of the examiner.^{3,6} Last, lymphangitis is rarely seen in necrotizing fasciitis as the primary site of pathology is in a deeper plane, i.e., in the deep fascia.^{3,12} Lymphangitis is seen more often in pathology around the lymphatic channels such as cellulitis where the infection lies in the deep dermis and subcutaneous tissue.

Correlation with systemic features of sepsis should be stressed. Systemic manifestations of necrotizing fasciitis with high fever, hypotension, prostration, and multi-organ failure are crucial diagnostic indicators.^{3,4,6} This is classically caused by superantigens elaborated by group A *Streptococcus* where it is known as streptococcal toxic shock syndrome.¹³ Green *et al.*³ listed fever and signs and symptoms of systemic toxicity as diagnostic features of necrotizing fasciitis. However, we are coming to appreciate that often, patients can appear systemically quite well, at least initially.² In a review of 89 consecutive patients, Wong *et al.*² found that only 53% were febrile and 18% were hypotensive at presentation. This is particularly so in immunocompromised patients such as diabetics. These patients may have a blunted immunologic response to infection and may appear well initially despite the presence of severe necrotizing infection. The widespread use of broad-spectrum antimicrobials at the primary care level has also been speculated to be responsible for the apparent lack of systemic manifestation of such severe soft-tissue infection, at least initially.^{2,14} The implications are twofold. First, patients with systemic toxicity and multi-organ function disturbances associated with nonspecific signs of soft tissue infection (erythema, tenderness, pain, and swelling) should be treated with a presumptive diagnosis of necrotizing fasciitis until proven otherwise (by imaging or surgical exploration). Second, the lack of systemic disturbance in patients being evaluated for soft-tissue infections does not exclude the possibility of necrotizing fasciitis and careful serial assessment must be made.

Bakleh *et al.*¹⁵ recently demonstrated correlation between histopathologic findings and mortality in patients with necrotizing fasciitis. In their retrospective study, the histopathology of necrotizing fasciitis was classified, based on hematoxylin and gram stains, into three histologic stages. Histologic stages 1-3 were characterized by progressively decreasing neutrophilic response or polymorphonuclear leukocytes infiltration and increasing bacterial proliferation. Stages 1, 2, and 3 were associated with a mortality of 7.1%, 14.2%, and 47%, respectively. This corresponded to increasing tissue ischemia with decreasing perfusion and increasing bacterial proliferation within the infected tissue specimen. The increased mortality noted from histologic stage 1 through 3 collaborates with the clinical observation of delayed surgical debridement and increased mortality reported by many authors.¹⁻¹⁰ In this present study, we have demonstrated that progressive tissue ischemia was reflected by progressive cutaneous skin changes. Although subtle, these changes will be evident to astute observers aware of its significance. Bakleh *et al.*'s study¹⁵ and our clinical observations supported the hypothesis that the underlying pathology of necrotizing fasciitis is a continuum of progressive tissue ischemia and liquefactive necrosis.

Limitation of this study is in its retrospective design, which introduces potential biases. Given the rarity of necrotizing

Table 5 The LRINEC score is calculated by summation of the six individual parameters. The maximum score is 13; a score of 6 or greater should raise the suspicion of necrotizing fasciitis and a score of 8 or greater is strongly predictive of this disease

Variable (units)	Score
C-reactive protein (CRP) (mg/L)	
< 150	0
150 or more	4
Total white cell count (per mm ³)	
< 15	0
15–25	1
> 25	2
Hemoglobin (Hb) (g/dL)	
> 13.5	0
11–13.5	1
< 11	2
Sodium (Na) (mmol/L)	
135 or more	0
< 135	2
Creatinine (Cr) (μmol/L)	
141 or less	0
> 141	2
Glucose (mmol/L)	
10 or less	0
> 10	1

Reproduced from Wong *et al.*²⁸

fasciitis, however, it is difficult to conduct a prospective study within a reasonable time frame. Also, the ethical issues involved in serial observation of cases of suspected necrotizing fasciitis are difficult to resolve. Diagnostic tests currently exist have been reported to be more sensitive than clinical examination alone. Modalities such as computed tomography (CT) scans or magnetic resonance imaging of the affected parts have been shown to be able to detect early necrotizing fasciitis.^{16–27} Other recently described diagnostic adjuncts that may be helpful include the laboratory risk indicator for necrotizing fasciitis (LRINEC) score.^{28–30} The LRINEC score, based on routinely available laboratory tests for assessment of severe soft-tissue infections, is a predictive model developed specifically to distinguish necrotizing fasciitis from other more benign soft-tissue infections such as cellulitis. The score is reported to be sensitive even for cases of early necrotizing fasciitis (Table 5). Although these tests are valuable diagnostic adjuncts in the assessment of severe soft-tissue infections, it must be reiterated that necrotizing fasciitis is a clinical diagnosis and clinical acumen remains crucial.

Conclusion

This study details the progressive skin changes as necrotizing fasciitis evolves. We have demonstrated that the cutaneous features of necrotizing fasciitis evolve from early (stage 1)

through an intermediate (stage 2) to late stage (stage 3). We hope these findings can serve as a guide in serial evaluation of severe soft-tissue infections and help in earlier recognition of necrotizing fasciitis by heightening awareness and the index of suspicion. Ultimately, when the diagnosis remains in doubt, immediate surgical exploration remains the standard of care.

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