Diagnosis and management of necrotizing fasciitis

Necrotizing fasciitis is a rapidly progressive, life-threatening soft tissue infection which is rapidly fatal unless diagnosed promptly and treated with immediate debridement of necrotic tissue. As early clinical suspicion is paramount to improved survival, this review aims to increase awareness of the condition.

Necrotizing fasciitis is an uncommon but severe life-threatening necrotizing soft tissue infection characterized by rapidly progressing inflammation and widespread fascial necrosis. It is distinct from common superficial skin infections such as impetigo and cellulitis which do not extend beyond the epidermis and dermis. Although first described by Hippocrates (Descamps et al, 1994) in the fifth century BC, the term necrotizing fasciitis was coined by Wilson in 1952 to describe the most consistent features of the disease: necrosis of the fascia and subcutaneous tissue with relative sparing of the underlying muscle. Although it can occur in any region of the body necrotizing fasciitis mostly occurs in the abdominal wall, extremities and perineum (Fournier's gangrene) (McHenry et al, 1994).

Necrotizing fasciitis is a surgical emergency. Rapid surgical debridement, parenteral antibiotics and aggressive fluid resuscitation are mainstays of therapy (Ustin and Malangoni, 2011). Regrettably the diagnosis is often delayed because of unfamiliarity with the condition and the initial paucity of skin findings (Hasham et al, 2005). As the diagnosis is essentially clinical, the opinion of surgeons experienced in the recognition and management of this uncommon condition should be sought immediately necrotizing fasciitis is suspected (Green et al, 1996).

Clinical presentation

Necrotizing fasciitis commonly presents as an erythematous, tender, swollen hot area of skin accompanied by localized pain and signs of systemic sepsis (Childers et al, 2002; Singh et al, 2002) (*Table 1*). The pain is typically disproportionately severe considering the size of the lesion and has been described as 'crescendo like' as progressive ischaemia and tissue infarction occur secondary to obliterative vasculitis. As lymph channels are obstructed early lymphadenitis and lymphangitis are rare. If left untreated the skin becomes progressively more tense and erythematous, with rapid migration of the margins. Crepitus may be present. Blisters and bullae then form and drain first serosanguinous and then haemorrhagic fluid, followed by eventual skin necrosis (Andreasen et al, 2001) (*Figure 1*).

Table 1. Key diagnostic features of necrotizing fasciitis

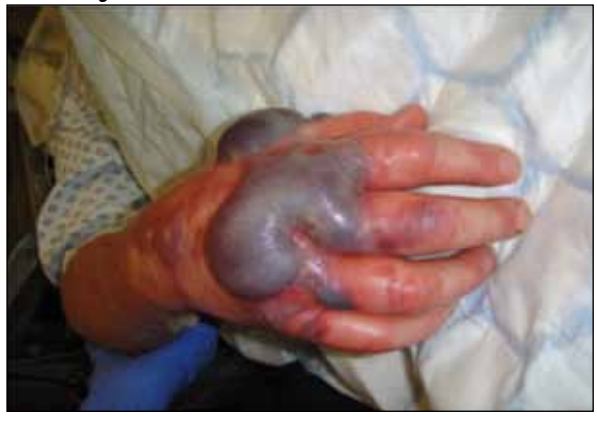
Erythema and swelling at affected site
Severe pain disproportionate to local findings
Signs of severe sepsis (e.g. tachycardia, hypotension, metabolic acidosis)

Epidemiology

The true incidence of necrotizing fasciitis in the UK is unknown as there are no ongoing surveillance programmes which capture data on cases of necrotizing fasciitis. Confusion surrounding the exact definition of necrotizing fasciitis and the plethora of terms used to describe the condition further hamper accurate reporting of the incidence.

Although necrotizing fasciitis can occur in previously healthy individuals the majority have comorbidities that render them susceptible to infection. Diabetes mellitus, the most common comorbidity, is present in 18–60% of cases. Other predisposing factors include intravenous

Figure 1. Advanced necrotizing fasciitis of the hand with haemorrhagic bullae and skin necrosis.



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drug abuse, chronic corticosteroid therapy, alcohol abuse, malnutrition and therapeutic immunosuppression (Sarani et al, 2009).

The reported mortality ranges from 6 to 76%, with death usually attributable to septic shock and multiorgan failure. The mortality rate is favourably influenced by rapid diagnosis and prompt aggressive surgical debridement (Wong et al, 2008).

Aetiology

Necrotizing fasciitis most commonly occurs after bacteria enter the subcutaneous space via any disruption of the overlying skin such as a laceration, abrasion or surgical incision. Even a very minor lesion may be sufficient to allow entry to bacteria and in a number of cases no identifiable cause can be found. Haematogenous spread from a distant site of infection has also been documented.

Histopathology

Necrotizing fasciitis is characterized by widespread necrosis of superficial fascia, subcutaneous fat, nerves, arteries and veins (Umbert et al, 1989). Microorganisms may be observed between collagen bundles and fat globules, and a dense polymorphonuclear infiltrate is present. As the disease advances myonecrosis may develop.

Microbiology

Numerous organisms have been implicated in the pathogenesis of necrotizing fasciitis and most cases of necrotizing fasciitis are polymicrobial (*Table 2*). Necrotizing fasciitis can be classified into four types based on wound microbiology (Morgan, 2010). Type I infections are characterized by polymicrobial infection and represent approximately 70–80% of all necrotizing fasciitis infections. Type II infections represent approximately 10–20% of cases and are defined by the presence of group A β-haemolytic streptococcus. Types III and IV are much less prevalent in the UK, the former being caused by Gram-negative marine-related organisms such as *Vibrio* spp. while type IV infections are fungal in nature and mainly affect the immunocompromised.

Table 2. Microbiology of necrotizing fasciitis: 162 organisms cultured from 73 patients with confirmed necrotizing fasciitis

Organism	No. of cases
Streptococcus spp.	31
Staphylococcus aureus	26
Klebsiella spp.	17
Enterococci	14
Acinetobacter baumanii	13
Escherichia coli	12
Pseudomonas aeruginosa	10
Enterobacter spp.	6
Proteus spp.	6
Bacteroides spp.	6
Fungi (*Candida* spp.)	5
Peptostreptococcus spp.	4
Clostridium spp.	2
Other	10

From Wong et al (2003)

According to data from the Department of Health (2009) the number of patients with invasive infections secondary to group A β-haemolytic streptococcus, including necrotizing fasciitis, is becoming more common. *Streptococcus pyogenes* or group A streptococcus is a Gram positive extracellular bacterial pathogen which is implicated in a number of pyogenic infections including necrotizing fasciitis. Streptococci can be serologically separated into M protein subtypes based on a surface protein (Cunningham, 2000). M proteins on the surface of the cell act to inhibit phagocytosis by polymorphonuclear leucocytes and inhibit neutrophil chemotaxis. Although multiple M types have been associated with necrotizing fasciitis, types M1 and M3 are the most prevalent. Group A β-haemolytic streptococcus also express a number of other virulence factors, the nature and function of which depend on the site of infection. These factors are crucial for colonization, adherence and evasion of the immune system. One such factor, streptococcal pyrogenic exotoxin, is encoded by the SpeB gene and is highly expressed at the site of tissue infection in patients with necrotizing fasciitis. Acting as a superantigen, this and other exotoxins induce T-cell activation leading to the release of cytokines and other pro-inflammatory mediators with a subsequent overwhelming inflammatory response (Olsen and Musser, 2010). Streptococci also release a range of other enzymes including haemolysins, DNAase, proteases and collagenases leading to destruction of surrounding tissues facilitating the spread of infection.

Clinical diagnosis

Early diagnosis is difficult as the cutaneous manifestations of the disease are often very limited. A high index of suspicion is required and if necrotizing fasciitis is suspected it is advisable to seek the opinion of a surgeon experienced in the recognition and management of the disease. Diagnostic clues include severe pain at the site of infection which is disproportionate to the extent of the lesion and signs of severe systemic infection (Chelsom et al, 1994). Frequent and repeated examination of the patient is required if there is any doubt about the diagnosis.

Recognizing the difficulties of differentiating necrotizing fasciitis from other less severe soft tissue infections, Wong et al (2004) proposed a novel, simple and objective scoring system, the Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score, based on routine

laboratory investigations (*Table 3*). This score is capable of detecting early cases of necrotizing fasciitis among patients with severe soft tissue infections. At a cut off of a LRINEC score of ≥6, the model has a positive predictive value of 92% (95% confidence interval = 84.3–96.0) and negative predictive value of 96% (95% confidence interval = 92.6–97.9). A score of ≥8 is strongly predictive of necrotizing fasciitis (positive predictive value 93.4%; 95% confidence interval = 85.5–97.2). Unfortunately the score has not yet been adequately prospectively validated, and the authors themselves advise early surgical intervention when the index of clinical suspicion is high.

Investigations

Although essentially a clinical diagnosis, imaging may usefully aid the diagnosis of necrotizing fasciitis provided that it does not delay surgery when a high index of suspicion exists. Plain X-ray may detect soft tissue gas although this is often a late sign of infection and not always present.

A retrospective study by Wysoki et al (1997) of 20 patients with confirmed necrotizing fasciitis suggested that computed tomography scanning may be useful in the diagnosis of necrotizing fasciitis. Asymmetric fascial thickening and fat stranding were seen in approximately 80% of cases and just over half of cases were found to have gas tracking along fascial planes. However, prospective studies examining the utility of computed tomography scanning in diagnosis necrotizing fasciitis are lacking.

Magnetic resonance imaging is useful in differentiating between necrotizing fasciitis and other soft tissue infections as it is capable of revealing contrast enhancement of soft tissues and is highly sensitive in the detection of fluid collections. Schmid et al (1998) performed magnetic resonance examination of 15 patients with clinically suspected necrotizing fasciitis and reported that necrotizing fasciitis can be excluded when no deep fascial involvement is revealed with magnetic resonance imaging. Magnetic resonance was highly sensitive for detecting necrotizing fasciitis (100%) but lacked specificity (86%), tending to overestimate the extent of deep fascial involvement. This lack of specificity suggests that although magnetic resonance imaging is extremely useful, imaging alone should not form the basis of clinical decision making.

Table 3. Laboratory Risk Indicator for Necrotizing Fasciitis

Variable (units)		Score
C-reactive protein (mg/litre)	<150	0
	≥150	4
Total white cell count (per mm^3)	<15	0
	15–25	1
	>25	2
Haemoglobin (g/dl)	>13.5	0
	11–13.5	1
	<11	2
Sodium(mmol/litre)	≥135	0
	<135	2
Creatinine (μmol/litre)	≤141	0
	>141	2
Glucose (mmol/litre)	≤10	0
	>10	1

A Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score of ≥6 should raise the suspicion of necrotising fasciitis, and a score of ≥8 is strongly predictive of the disease. From Wong et al (2004)

Treatment

Patients with suspected necrotizing fasciitis should be admitted to a critical care area with appropriate expertise and facilities for invasive haemodynamic monitoring. Aggressive surgical management, intravenous antibiotics and supportive care form the mainstays of treatment.

Antibiotics

Rapid, appropriate intravenous antibiotic administration is central to the management of necrotizing fasciitis. Although adjunctive to surgical debridement, early suitable antibiotic therapy reduces mortality from severe sepsis and septic shock (Kumar et al, 2006). As necrotizing fasciitis is commonly polymicrobial initial empirical therapy should be broadly active against a wide range of potential micro-organisms including Gram-positive cocci, facultative anaerobic Gram-negative rods and anaerobes (Morgan, 2010). Subsequent de-escalation of antibiotic therapy may be possible when the results of tissue and blood cultures become available.

No evidence-based guidelines on the optimal antibacterial management of necrotizing fasciitis exist, and it is recommended that the hospital microbiologist is consulted for advice. A carbapenem in combination with clindamycin provides coverage against the majority of likely organisms. Other alternative regimens include a combination of a broad spectrum β-lactam such as piperacillin-tazobactam with clindamycin and ciprofloxacin (Stevens et al, 2005). Clindamycin is recommended in all empirical antibiotic regimens as it has demonstrated mortality benefit in necrotizing fasciitis secondary to *Strep. pyogenes* (Mulla, 2004). Clindamycin is a bacteriostatic antibiotic with high bioavailability and good tissue penetration. The rationale for clindamycin inclusion is based on its ability to suppress production of group A β-haemolytic streptococcus exotoxins and cytokine production and enhanced phagocytosis of group A β-haemolytic streptococcus by M-protein synthesis inhibition. Confirmed infection with group A β-haemolytic streptococcus alone should be treated with benzylpenicillin and clindamycin.

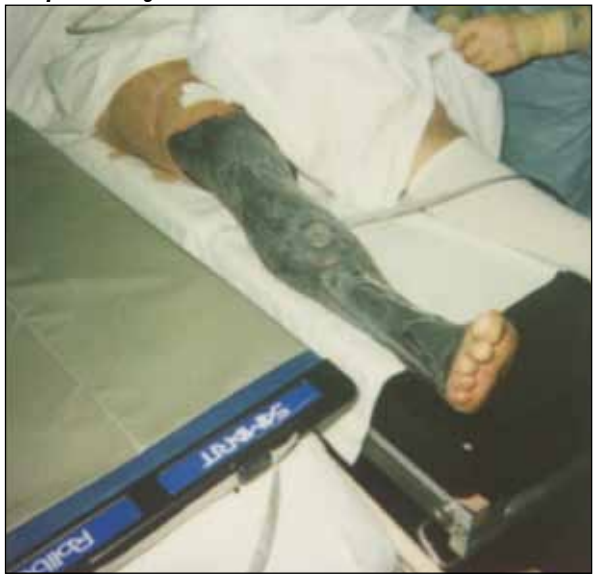
Surgery

Patients suspected of having necrotizing fasciitis should be taken to the operating theatre without delay for extensive debridement of all necrotic and devitalized tissue. Incisions to the deep fascia often reveal the presence of murky 'dishwater fluid' in the wound and all non-viable tissue including fascia should be removed. Tissue that can be easily separated from deep fascia with gentle finger dissection should be excised, and debridement should only halt when viable, vascularized tissue is encountered (Wong et al, 2008). Radical, disfiguring surgery is often required as thorough debridement is essential and associated with a reduction in mortality (Bilton et al, 1998). Further surgical examination of the affected area should be performed within 48 hours or sooner if indicated to ensure the adequacy of initial debridement. Multiple trips to theatre are commonly necessary. Elliott et al (1996) reported a series of patients with necrotizing fasciitis who underwent an average of 3.8 debridements per patient.

Vacuum-assisted closure therapy is routinely used after debridement to promote tissue wound healing (*Figure 2*). Briefly, a resilient, open cell foam surface dressing is applied to the wound and a wound drain with lateral perforation laid on top of it. The entire area is then covered with a transparent adhesive membrane, and the end of the drain attached to a specially designed commercially available pump (VAC, KCI, Kidlington, UK). Negative pressure is applied to the wound which increases localized blood flow by decreasing interstitial fluid, localized oedema and tissue bacterial counts. This promotes angiogenesis and the formation of granulation tissue.

Reconstructive surgery should only be considered when the patient has made a good recovery from the acute illness, and infection has been fully eradicated.

Figure 2. Application of a vacuum-assisted closure therapy system to a patient's leg after extensive debridement.



Adjunctive therapies

Hyperbaric oxygen therapy

Hyperbaric oxygen therapy is the delivery of 100% oxygen while under increased atmospheric pressure resulting in an elevated partial pressure of oxygen in tissues. Its application may be a useful adjunct to surgical debridement and antibiotic therapy in cases of necrotizing fasciitis as it is toxic to anaerobic bacteria and improves polymorphonuclear function and bacterial clearance (Cohn, 1986). Although there are a number of small retrospective studies suggesting benefit there are no high quality prospective trials examining its use in cases of necrotizing fasciitis, and its use remains controversial. Additionally, the lack of facilities in the UK and the logistic problems of managing a critically ill patient in a hyperbaric chamber mean that hyperbaric oxygen therapy is rarely used to manage patients with necrotizing fasciitis.

Intravenous immunoglobulin

Intravenous immunoglobulin is potentially of benefit in necrotizing fasciitis caused by group A β-haemolytic streptococcus because of its ability to opsonize bacteria and neutralize super-antigen toxins. However, its effectiveness remains to be vigorously established. Guidelines from the Department of Health (2008) suggest that intravenous immunoglobulin may be added to adequate toxin neutralizing antimicrobials, source control and sepsis management when these approaches have failed to elicit a response.

Conclusions

Necrotizing fasciitis is a life-threatening soft tissue infection characterized by widespread fascial necrosis with relative sparing of skin and underlying muscle. The initial paucity of clinical signs and symptoms often leads to delays in diagnosis and management. Diagnostic clues include severe pain disproportionate to the size of the lesion, and signs and symptoms of severe sepsis. A high index of suspicion is required and the opinion of a clinician experienced in the management of this condition should be sought immediately as the diagnosis is primarily a clinical one. Left untreated, it is usually rapidly fatal with the brisk onset of septic shock and multi-organ failure.

After initial resuscitation and the administration of empirical broad spectrum antibiotics, immediate surgical debridement of all devitalized tissue is mandatory. A return to theatre should be scheduled within 24 hours for wound inspection and further debridement of necrotic tissue if required. Vacuum-assisted closure therapy is often useful for wound coverage. The role of adjunctive therapies such as hyperbaric oxygen and intravenous immunoglobulins remains uncertain. **BJHM**

Conflict of interest: none.

Andreasen TJ, Green SD, Childers BJ (2001) Massive infectious soft-tissue injury: diagnosis and management of necrotizing fasciitis and purpura fulminans. *Plast Reconstr Surg* **107:** 1025–35
Bilton BD, Zibari GB, McMillan RW, Aultman DF, Dunn G, McDonald JC (1998) Aggressive surgical management of necrotizing fasciitis serves to decrease mortality: a retrospective study. *Am Surg* **64:** 397–400
Chelsom J, Halstensen A, Haga T, Høiby EA (1994) Necrotising fasciitis due to group A streptococci in western Norway: incidence and clinical features. *Lancet* **344**: 1111–15
Childers BJ, Potyondy LD, Nachreiner R et al (2002) Necrotizing fasciitis: A fourteen-year retrospective study of 163 consecutive patients. *Am Surg* **68:** 109–16
Cohn GH (1986) Hyperbaric oxygen therapy: promoting healing in difficult cases: *Postgrad Med* **79:** 517–28
Cunningham MW (2000) Pathogenesis of group A streptococcal infections. *Clin Microbiol Rev* **13:** 470–511
Department of Health (2008) *Clinical guidelines for immunoglobulin use.* Department of Health, London
Department of Health (2009) *Increase in invasive group A streptococcal infections in England.* Department of Health, London
Descamps V, Aitken J, Lee MG (1994) Hippocrates on necrotising fasciitis. *Lancet* **344:** 718–28
Elliott DC, Kufera JA, Myers RA (1996) Necrotizing soft tissue infections. Risk factors for mortality and strategies for management. *Ann Surg* **224:** 672–83
Green RJ, Dafoe DC, Raffin TA (1996) Necrotising fasciitis. *Chest* **110:** 219–29
Hasham S, Matteucci P, Stanley PRW, Hart NB (2005) Necrotising fasciitis. *BMJ* **330***:* 830–3
Kumar A, Roberts D, Wood KE et al (2006) Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. *Crit Care Med* **34:** 1589–96
McHenry CR, Brandt CP, Piotrowski JJ, Jacobs DG, Malangoni MA. (1994) Idiopathic necrotizing fasciitis: recognition, incidence, and outcome of therapy. *Am Surg* **60:** 490–4
Morgan MS (2010) Diagnosis and management of necrotising fasciitis: a multiparametric approach. *J Hosp Infect* **75:** 249–57
Mulla ZD (2004) Treatment options in the management of necrotising fasciitis caused by Group A Streptococcus. *Expert Opin Pharmacother* **5:** 1695–700
Olsen RJ, Musser JM (2010) Molecular pathogenesis of necrotizing fasciitis. *Ann Rev Pathol Mech Dis* **5:** 1–31
Sarani B, Strong M, Pascual J et al (2009) Necrotizing fasciitis: Current concepts and review of the literature. *J Am Coll Surg* **208:** 279–88
Schmid MR, Kossmann T, Duewell S (1998) Differentiation of necrotizing fasciitis and cellulitis using MR imaging. *Am J Roentgenol* **3:** 615–20
Singh G, Sinha SK, Adhikary S, Babu KS, Ray P, Khanna SK (2002) Necrotising infections of soft tissue – a clinical profile. *Eur J Surg* **168:** 366–71
Stevens DL, Bisno AL, Chambers HF et al (2005) Practice guidelines for the diagnosis and management of skin and soft-tissue infections. *Clin Infect Dis* **41:** 1373–406
Umbert IJ, Winkelmann RK, Oliver GF, Peters MS (1989) Necrotizing fasciitis: a clinical, microbiologic, and histopathologic study of 14 patients. *J Am Acad Dermatol* **20:** 774–81
Ustin J, Malangoni M (2011) Necrotizing soft tissue infections. *Crit Care Med* **39:** 1–8
Wilson B (1952) Necrotizing fasciitis. *Am Surg* **18:** 416–31
Wong CH, Chang HC, Pasupathy S, Khin LW, Tan JL, Low CO (2003) Necrotizing fasciitis: clinical presentation, microbiology, and determinants of mortality. *J Bone Joint Surg Am* **85-A**(8): 1454–60
Wong CH, Khin LW, Heng KS, Tan KC, Low CO (2004) The LRINEC (Laboratory Risk Indicator for Necrotizing Fasciitis) score: a tool for distinguishing necrotizing fasciitis from other soft tissue infections. *Crit Care Med* **32:** 1535–41
Wong CH, Yam AK, Tan AB, Song C (2008) Approach to debridement in necrotizing fasciitis. *Am J Surg* **196:** 19–24
Wysoki MG, Santora TA, Shah RM, Friedman AC (1997) Necrotizing fasciitis: CT characteristics. *Radiology* **203:** 859–63

KEY POINTS

- Necrotizing fasciitis is a surgical emergency.
- Diagnosis is primarily clinical and requires a high index of suspicion. Severe pain, localized erythema or swelling and signs of systemic sepsis are the usual clinical findings.
- Rapid aggressive surgical debridement is the primary means of treating necrotizing fasciitis.