BRITISH JOURNAL OF HOSPITAL MEDICINE

REVIEW

Necrotising fasciitis: a narrative review of the literature

Josiah Damisa[1]

Sohail Ahmed[1]

Sanjay Harrison[1]

Author details can be found at the end of this article

Correspondence to:
Josiah Damisa;
josiahdamisa@googlemail.com

Abstract

Necrotising fasciitis is a severe, life-threatening and rapidly progressive soft tissue infection that often requires aggressive surgical management, with an estimated incidence of about 0.24–0.40 per 100 000 in the UK. Necrotising fasciitis can be classified based on its microbiology or the anatomy or body region affected.

Initial signs of necrotising fasciitis can be minimal and non-specific but a patient often presents with pain out of proportion to clinical signs on examination, as well as erythema and oedema, in addition to systemic symptoms associated with sepsis.

Diagnosis is often based on high clinical suspicion with biochemical and clinical imaging used as adjuncts. To aid with early diagnosis of necrotising fasciitis, a scoring system known as the Laboratory Risk Indicator for necrotising fasciitis was developed which has a positive predictive value of 92%. Once diagnosed, appropriate resuscitation and antibiotics, along with prompt and aggressive surgical debridement, is the mainstay of treatment.

Key words: Broad spectrum antibiotics, Debridement, Laboratory Risk Indicator for necrotising fasciitis, Necrotising fasciitis, Resuscitation, Skin infection

Received: 24 September 2020; accepted following double-blind peer review: 2 December 2020

Introduction

Necrotising fasciitis is a severe, life-threatening and rapidly progressive soft tissue infection, which primarily affects superficial fascia. It often requires immediate aggressive surgical management through extensive debridement (Kückelhaus et al, 2017), as any delay often proves fatal as it progresses to septic shock.

This condition received considerable media attention in the mid-1990s when an outbreak occurred in Gloucester, and it came to be known as the 'flesh-eating disease'.

While rare, the devastating clinical sequelae of necrotising fasciitis has been present for millennia, described as early as 500 BC by Hippocrates. The term necrotising fasciitis was first used by Wilson (1952).

Notorious for high morbidity and mortality, these rates have largely remained unchanged for the last 30 years (Sarani et al, 2009).

Epidemiology

Estimating the incidence of necrotising fasciitis in the UK has proven difficult as it is not a notifiable disease, with scant public records. However, some reports estimate the incidence of necrotising fasciitis to be around 0.24–0.40 per 100 000 and more recent data indicate that 500 new cases per year in the UK are diagnosed (Hasham et al, 2005; Morgan, 2010). Reports suggest an increasing incidence over the last two decades, probably as a result of the emergence of more virulent strains of bacteria (Rogers et al, 2007; Krapp et al, 2017).

How to cite this article:
Damisa J, Ahmed S, Harrison S. Necrotising fasciitis: a narrative review of the literature. Br J Hosp Med. 2021. https://doi.org/10.12968/hmed.2020.0577

Classification

Necrotising fasciitis can be classified by microbiology or anatomy.

Anatomy

A commonly used eponym for perineal necrotising fasciitis is 'Fournier's gangrene'. A study by Chen et al (2017), in a series of 60 patients, found the pelvis to be the most common

site of necrotising fasciitis (28%), closely followed by the lower extremity (27%), trunk (23%), and upper extremity (17%). Three out of 60 patients in this series had more than one affected region, of which the mortality rate was 100%.

Sarani et al (2009) argue for the term 'necrotising soft tissue infection', which is also used in the literature. This expression reflects that a final common diagnostic and management pathway for all types of necrotising fasciitis negates any need for terminological debate or classification. Sarani et al (2009) suggested that classification systems may be detrimental as this delays prompt recognition and timely surgical intervention.

Microbiology

Necrotising fasciitis can also be classified by causative organism, initially classified into two subtypes: polymicrobial (type I) or monomicrobial (type II). This classification system has been expanded more recently to include types III and IV (Table 1), although there is yet to be universal consensus regarding these new additions (Morgan, 2010). Type III and IV are rare, while types I and II are more common in the UK (Davoudian and Flint, 2012).

Type I necrotising fasciitis accounts for the majority of cases and results from polymicrobial infection with anaerobic, aerobic and facultative anaerobic bacteria. It is most commonly found in immunocompromised patients (eg those with diabetes, HIV, intravenous drug users, as well as alcoholics, and patients on chemotherapy) or those with predisposing abdominal pathology. The usual organisms are *Escherichia coli*, *Pseudomonas aeruginosa* and *Bacteroides* spp, which normally affect the perineum and trunk (Puvanendran et al, 2009).

Type II necrotising fasciitis is often a monomicrobial infection, most commonly group A streptococcus, but occasionally in conjunction with *Staphylococcus aureus*. It is associated with a considerably higher mortality rate, as some patients may have streptococcal toxic shock syndrome, a precursor to multiorgan failure (Davoudian and Flint, 2012). It classically occurs in the extremities, especially in individuals who have undergone recent surgery or trauma but who are otherwise healthy, young and immunocompetent.

Type III necrotising fasciitis is commonly caused by a gram negative bacteria, a monobacterial infection usually caused by *Vibrio* spp, acquired if breaks in the skin are exposed to warm sea water and marine life. It is very rare but often has a fulminant course associated with multiorgan failure (Davoudian and Flint, 2012). Patients with moderate to severe liver disease are particularly at risk, with several factors accounting for this, some of which include decreased phagocytic activity and low complement levels, but also increased bacterial translocation from the intestines via the intestinal portal route in patients with cirrhosis secondary to viral hepatitis, compared to non-cirrhotic patients (Hung et al, 2014; Bhat et al, 2019).

Type IV necrotising fasciitis is caused by fungal infections and usually develops following burns and traumatic wounds. Candidal infections occur mainly in immunocompromised patients but zygomycosis (*Mucor, Rhizopus*) tends to occur in immunocompetent individuals (Davoudian and Flint, 2012).

Table 1. Microbiological classification of necrotising fasciitis

Type of necrotising fasciitis	Aetiology	Organism(s)
Type I	Polymicrobial and synergistic infection, usually bowel-related organisms	Mixed anaerobes and aerobes
Type II	Monomicrobial, initial infection usually from the throat or skin	Group A streptococcus with or without co-existing *Staphylococcus aureus*
Type III	Gram negative, usually marine-related organisms	Predominantly *Vibrio* spp
Type IV	Usually following trauma, can occur in immunocompetent or immunocompromised individuals	Candida (immunocompromised), Zygomycetes (immunocompetent)

From Davoudian and Flint (2012)

Pathophysiology

In type I necrotising fasciitis, the initial polymicrobial infection usually occurs following a minor penetrative injury. In high-risk patients, such as those with diabetes or arteriopathy, the haematogenous spread of enteric organisms can result in necrotising fasciitis of vulnerable tissue. The terms used in older literature such as 'Fournier's gangrene' or 'Melaney's gangrene' are classifications based on anatomical site and can lead to confusion, even though the treatment for these conditions is the same. Intravenous drug users are at a high risk of developing necrotising fasciitis, usually by the direct introduction of the organism via contaminated needles.

The organisms rapidly multiply and spread, only limited by the fibrinous attachments of the fascia to deep tissue. Breaching of the fascia can result in myositis. Proliferation of the pathogens results in thrombosis of the blood vessels in the dermal papillae, eventually leading to ischaemia and gangrene of the subcutaneous fat and dermis. The subcutaneous emphysema characteristic of necrotising fasciitis is only seen when there is infection by gas-producing organisms such as *Clostridium perfringens* and other less common *Clostridium* species (Bonne, 2017).

Entry of group A streptococcus into the sub-dermal layer via microtrauma results in type II necrotising fasciitis. The infecting group A streptococcus is very often carried by the patient asymptomatically. The M protein expressed by certain strains of group A streptococcus increases the pathogen's ability to adhere to tissue and protects it against phagocytosis. Secreted exotoxins (A and B) act as superantigens stimulating massive T-cell proliferation, releasing cytokines and inflammatory mediators culminating in a systemic inflammatory response. The resultant increased capillary permeability and profound hypotension can progress to shock, multiorgan dysfunction and streptococcal toxic shock syndrome. The streptococci also release large amounts of degradative enzymes, which undermine the overlying skin resulting in coagulative necrosis. This in turn creates an environment conducive to bacterial multiplication and spread (Olsen and Musser et al, 2010).

Types III and IV are rare and often implicated in immunocompromised individuals. Once the invading organisms access the subdermal layer, the pathophysiology progresses very similarly to type I necrotising fasciitis.

Symptoms and assessment

The classical symptoms of necrotising fasciitis have been described as erythema, oedema and pain out of proportion to the signs. However, these signs are easily mistaken for non-necrotising infections and therefore present a diagnostic challenge to most physicians. Furthermore, in patients with diabetic neuropathy, the experience of pain might be less, masking the seriousness of the condition. Once necrotising fasciitis is established, ischaemia means that there is no erythema of the overlying skin and necrosis sets in (Figure 1) (Goh et al, 2014).

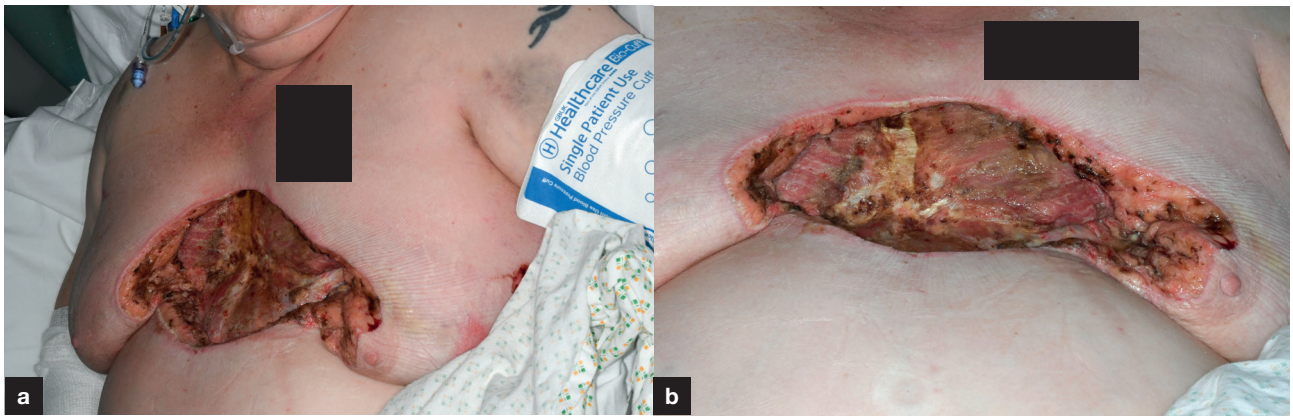

Figure 1. A 52-year-old woman with known Addison disease and type 2 diabetes mellitus presented with a chest injury and noted necrotic slough sustained after an innocuous injury 3 days earlier from falling on a table. Initial extensive debridement was required. a. Day 12 post-debridement – side view. b. Day 12 post-debridement – frontal view.

The progressive coagulative necrosis of the fascia results in extreme pain experienced by these patients. Most commonly, in the early stages of necrotising fasciitis there are no obvious skin changes. There is usually a history of local trauma or muscle strain. Sometimes the only symptom may be a pyrexia of unknown origin in a hospital patient, which would therefore warrant a thorough physical examination.

Systemic symptoms such as pyrexia, hypotension, tachycardia and tachypnoea are usually present, although their absence does not rule out underlying necrotising fasciitis. As the condition progresses the dermal ischaemia manifests itself as ecchymotic lesions and haemorrhagic bullae (Kiat et al, 2017). These bullae are highly suggestive of necrotising fasciitis and should prompt further action on behalf of the physician. Further progression leads to tissue loss.

Bakleh et al (2005), in a series of 82 cases, described characteristic surgical findings including grey discolouration of fascia, ease of blunt dissection along tissue planes and the absence of bleeding alongside malodourous 'dishwater' pus.

Owing to the diagnostic difficulties associated with necrotising fasciitis, Wong et al (2004) developed a scoring system known as the Laboratory Risk Indicator for Necrotising Fasciitis (LRINEC). If a patient has a score of 6 or above out of a possible 13 from the criteria shown in Table 2, this is highly suggestive of necrotising fasciitis, with a positive predictive value of 92% and a negative predictive value of 96%.

However, despite the score clinical acumen that should prevail and urgent surgical referral should be arranged if necrotising fasciitis is suspected.

There is controversy regarding the link between the use of non-steroidal anti-inflammatory drugs and risk of necrotising fasciitis caused by invasive group A streptococcus infections. Some studies suggest an increased risk perhaps as a result of non-steroidal anti-inflammatory drugs masking the early inflammatory reaction in necrotising fasciitis. Therefore, some authors advocate stopping all non-steroidal anti-inflammatory drugs in patients with suspected necrotising fasciitis (Das et al, 2012). However, Aronoff and Bloch (2003) argue that there is no established link between the use of non-steroidal anti-inflammatory drugs and increased risk of necrotising fasciitis caused by group A streptococcus.

Table 2. The Laboratory Risk Indicator for Necrotising Fasciitis (LRINEC) score

Parameter	Value	Score
C-reactive protein (mg/litre)	Less than 150	0
	More than 150	4
White cell count (per mm^3)	Less than 15	0
	15–25	1
	More than 25	2
Haemoglobin (g/dl)	More than 13.5	0
	11–13.5	1
	Less than 11	2
Sodium (mmol/litre)	More than or equal to 135	0
	Less than 135	2
Creatinine (µmol/litre)	Less than or equal to 141	0
	More than 141	2
Glucose (mmol/litre)	Less than or equal to 10	0
	More than 10	1

From Wong et al (2004)

Investigations

When a patient presents with symptoms suggestive of necrotising fasciitis, routine observations and blood tests including their inflammatory markers and blood glucose levels should be checked. These results also enable the patient to be scored according to the LRINEC system. An elevated creatine phosphokinase level might indicate muscle damage caused by bacteria breaching the fascia (Davoudian and Flint, 2012; Bechar et al, 2017).

With necrotising fasciitis often a precursor of sepsis, there is a promising role for arterial blood gas tests being used as an adjunct diagnostic tool, with Murphy et al (2013) in a prospective study of 53 patients showing that raised serum lactate levels over 2.0 mmol/litre are strongly associated with the presence of tissue necrosis.

Radiological imaging is used primarily as an adjunct to clinical diagnosis. Point of care ultrasound has been a useful diagnostic tool in necrotising fasciitis, especially when the diagnosis is still unclear. Sonographic imaging has proved a valuable tool in differentiating between necrotising fasciitis and cellulitis, as both conditions have diffuse thickening of overlying fatty tissue and deep fascia. In necrotising fasciitis, there is a characteristic fluid layer tracking along the deep fascia and soft tissue gas noted when ultrasound imaging is performed, with Lin et al (2019) showing that a fluid accumulation level of more than 2 mm depth had an accuracy of 72.7%.

Plain radiographs are only useful in detecting gas in the subcutaneous tissue. While subcutaneous emphysema is very characteristic of necrotising fasciitis, it is only present in a minority of patients and therefore the use of plain radiographs is very limited. The absence of subcutaneous emphysema on plain radiograph does not exclude necrotising fasciitis (Fernando et al, 2019).

Computed tomography is more sensitive and, in addition to subcutaneous emphysema, can also show the characteristic changes of inflammation such as oedema, abscesses or fascial thickening (Figure 2) (Fernando et al, 2019).

Magnetic resonance imaging is often the preferred choice of imaging for detailed evaluation of soft tissue infection because of its high spatial and contrast resolution, as it allows for the estimation of the degree of involvement of soft tissue and underlying bone. T1-weighted sequences have shown evident circumferential dermal and soft tissue thickening (Chaudhry et al, 2015). However, its use might not always be appropriate in critically ill or unstable patients as it can lead to delays in management. Computed tomography scans are typically more widely available and do not usually result in delays.

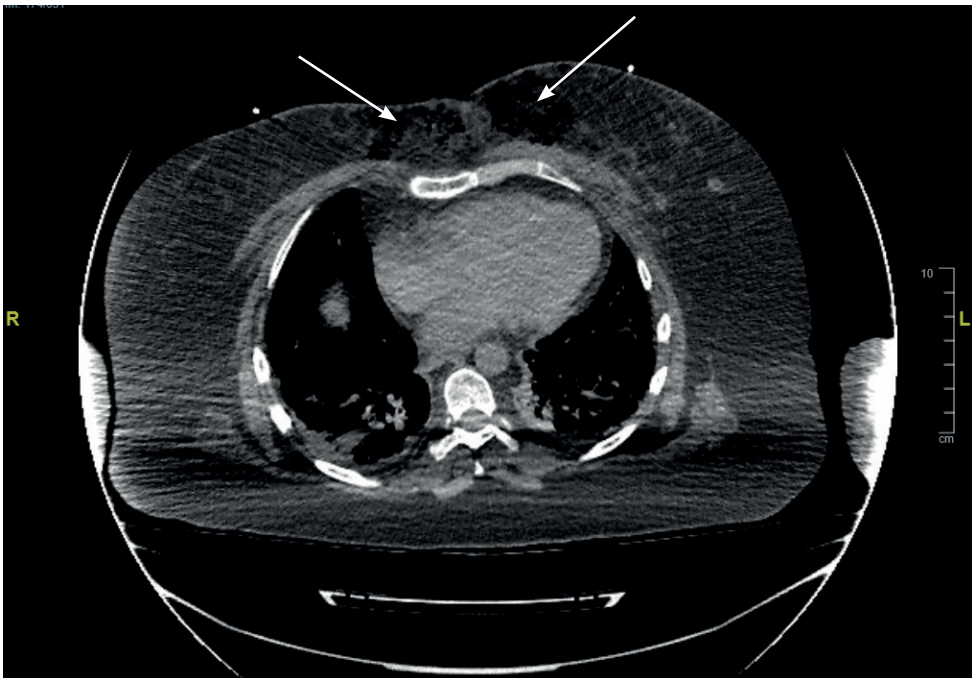

Figure 2. Computed tomography scan of the patient in **Figure 1**. Note the presence of gas in the soft tissues as indicated by the arrows.

A historical diagnostic modality previously used at the bedside, but no longer used as a definitive test, is the 'finger test'. In this test, after local anaesthetic infiltration, a 2 cm incision is made down to the deep fascia and the wound is probed gently with the index finger. The presence of characteristic 'dishwater pus', a lack of bleeding and a lack of resistance from the tissue to blunt dissection are all signs highly suggestive of necrotising fasciitis. Any fluid or pus obtained during this procedure can be sent for Gram stain, culture and sensitivity testing (Maya et al, 2014).

Management

Shocked patients require appropriate resuscitative measures such as intravenous fluids and possibly inotropes. The use of antibiotics is important in combating the systemic sepsis and microbial spread. Although the choice of antibiotics can be guided by Gram stain, the fulminant nature of necrotising fasciitis makes broad spectrum empirical therapy a sensible option. Historically, the antibiotic regimen of choice was high dose penicillin and clindamycin which covered Gram positive and anaerobic organisms (Bonne et al, 2017).

With the emergence of varying antibiotic resistance among pathogens and newer causative agents, lipoglycopeptides, such as vancomycin, are very effective in treating necrotising fasciitis, especially for patients requiring short hospital stays and early discharge (Menichetti et al, 2017). Clindamycin remains a useful drug because it blocks synthesis of exotoxins by group A streptococcus. Quinolones can be used for Gram negative coverage and also possess good soft tissue penetration. There is no consensus on the duration of antibiotic use but it is generally used until no further surgical intervention is required and there are no more signs of inflammation (Hunter et al, 2011; Peetermans et al, 2020).

Surgical management

The thrombogenic pathology of necrotising fasciitis prevents adequate penetration of intravenous antibiotics to the site of infection and definitive treatment is only achieved with surgical debridement (Bonne et al, 2017). The timing of surgery is vital and the more surgery is delayed, the higher the mortality associated with necrotising fasciitis. A study by Wong et al (2004) showed a delay of 24 hours before surgery was associated with a cumulative survival rate of 93.2% (95% confidence interval (86.6–99.8), which further declined to 75.2% (95% confidence interval 62.0–88.4) when the delay was prolonged further by 48 hours (Wong et al, 2004; Goh et al, 2014).

Aggressive surgical debridement is vital and should be continued until healthy bleeding tissue edges are reached. If aggressive enough, one debridement should be sufficient but in some cases several debridements, each 24 hours apart, are required to achieve a satisfactory result. The use of hydrogen peroxide wound washing, followed by saline rinse, can be considered, but not until the debridement is considered complete as it can make ischaemic tissue look healthy. Dressing changes at 24–48-hour intervals may require a general anaesthetic, at least initially. Vacuum-assisted closure dressing is now routinely preferred to conventional gauze dressing as it results in fast and effective wound closure (Moues et al, 2006). By providing an airtight environment through the continuous negative pressure, it improves wound healing by reducing localised oedema, absorbing excess exudate, encouraging granulation (Figure 3) and approximating the wound edges together (Misiakos et al, 2014) .

Amputation should be considered where extensive necrotising fasciitis has spread to the deeper tissue and rendered the affected limb useless, or if the infection is spreading towards the torso. Perianal, perineal and scrotal necrotising fasciitis may require a temporary diverting colostomy to aid wound healing (Peetermans et al, 2020).

When debridement is completed, and it is confirmed at 48 hours that no further debridement is necessary because of the absence of necrotic tissue, the wound may be closed by primary intention. Larger wounds may require reconstructive surgery using biological implants such as porcine collagen and assistance from the plastic surgeons using skin grafts (Figure 4) or flaps.

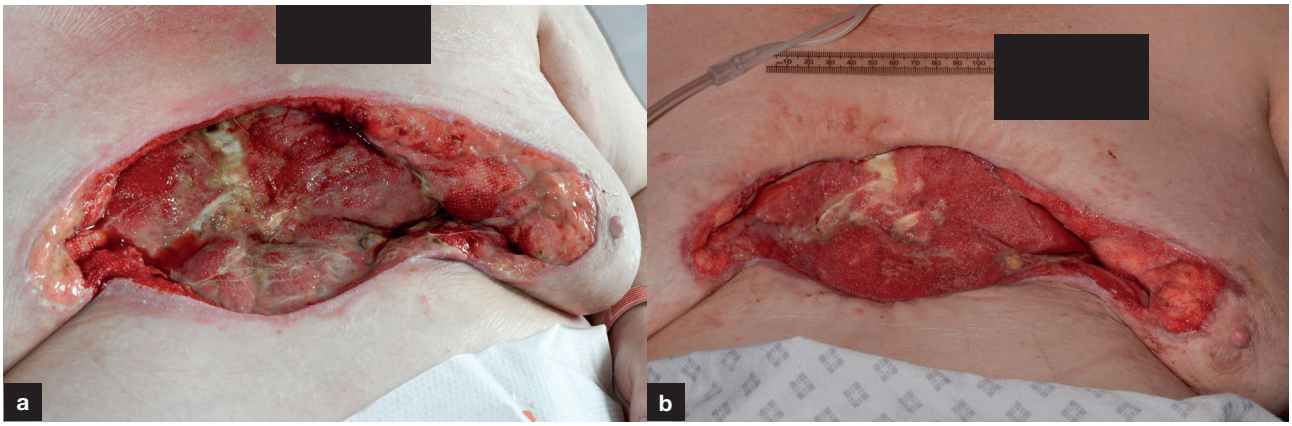

Figure 3. a. Patient in **Figure 1** 19 days post debridement with early signs of granulation following grafting. b. 35 days post debridement with evident granulation following grafting.

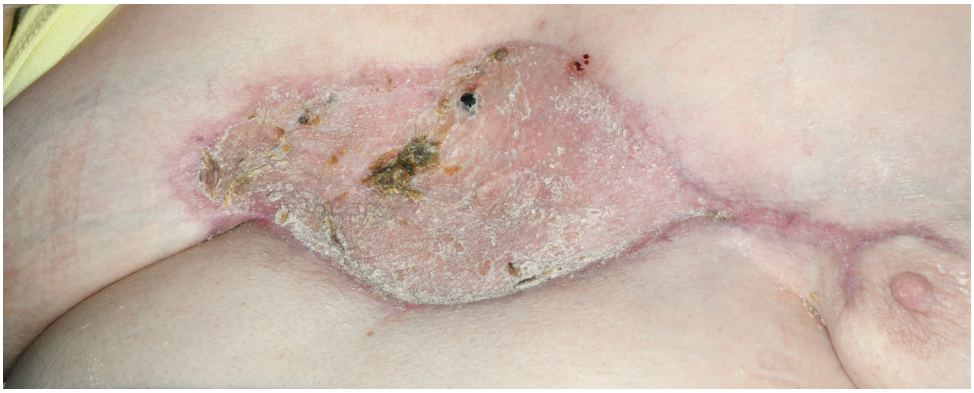

Figure 4. Healed skin tissue following grafting of patient in **Figure 1**.

The use of hyperbaric oxygen therapy is based on a high arterial oxygen tension inhibiting anaerobic bacterial growth and enhancing the oxygen-dependent killing ability of leucocytes. However, there is no conclusive evidence about the effects of hyperbaric oxygen therapy in reducing mortality (Peetermans et al, 2020). The use of intravenous immunoglobulin therapy to neutralise group A streptococcus toxins has been advocated by some but, again, larger trials are required to confirm a therapeutic benefit (Morgan, 2010).

Nutritional support is often indicated in severe cases of necrotising fasciitis. The high metabolic demands of necrotising fasciitis are similar to those of major trauma or burns and hence the lost proteins and fluids need to be replaced (Misiakos et al, 2014).

Prognosis

Mortality rates for necrotising fasciitis have been reported to vary between 20% and 75% (Cheung et al, 2009), with Goh et al (2014) reporting a median mortality ratio of 25.1%. The greatest predictor of mortality appears to be delay in taking the patient to theatre, normally the result of a delay in diagnosis. A prolongation of this time has been associated with a worse outcome. In cases of necrotising fasciitis with an invasive group A streptococcus infection and associated streptococcal toxic shock syndrome, the mortality rate has been reported to be as high as 67% (Simonart, 2004). Other factors such as an age greater than 65 years, leukopenia, hypotension and a high APACHE II score have also been associated with a higher mortality (Yaşar et al, 2017).

Conclusions

Necrotising fasciitis is a serious condition, complicated by the fact that the initial signs are minimal and usually non-specific. This often leads to delays in surgical management, which is correlated with a worse outcome. The key to diagnosing necrotising fasciitis is

Key points

- High clinical suspicions is the mainstay of diagnosis of necrotising fasciitis with investigations used as adjunts.
- Early resuscitation is vital as hypotension can be profound.
- Early input of high dependency and intensive care teams is recommended.
- Extensive surgical debridement is the definitive treatment.
- Delay in surgery for longer than 24 hours is associated with significant mortality.

taking a thorough history, performing repeated examination and maintaining a high index of clinical suspicion. Radiological investigations are useful adjuncts but by no means specific. Once diagnosed, appropriate resuscitation and antibiotics along with prompt and aggressive surgical debridement is the mainstay of treatment.

More research is needed to fully evaluate the role of therapeutic adjuncts such as hyperbaric oxygen therapy and intravenous immunoglobulin therapy. Also, the emergence of more virulent and resistant pathogenic organisms is a growing concern and is therefore a potential area in which further research should be focused.

Author details

[1]Department of General Surgery, Darlington Memorial Hospital, Darlington, UK.

Acknowledgement

The authors would like to thank the patient for use of her case in this article.

Conflicts of interest

The authors declare that there are no conflicts of interest.

References

Aronoff DM, Bloch KC. Assessing the relationship between the use of nonsteroidal antiinflammatory drugs and necrotizing fasciitis caused by group A streptococcus. Medicine (Baltimore). 2003;82(4):225–235. https://doi.org/10.1097/01.md.0000085060.63483.bb

Bakleh M, Wold LE, Mandrekar JN et al. Correlation of histopathologic findings with clinical outcome in necrotizing fasciitis. Clin Infect Dis. 2005;40(3):410–414. https://doi.org/10.1086/427286

Bechar J, Sepehripour S, Hardwicke J, Filobbos G. Laboratory risk indicator for necrotising fasciitis (LRINEC) score for the assessment of early necrotising fasciitis: a systematic review of the literature. annals. 2017;99(5):341–346. https://doi.org/10.1308/rcsann.2017.0053

Bhat P, Bhaskar M, Sistla S, Kadhiravan T. Fatal case of necrotising fasciitis due to Vibrio vulnificus in a patient with alcoholic liver disease and diabetes mellitus. BMJ Case Rep. 2019;12(1):bcr-2018-227851. https://doi.org/10.1136/bcr-2018-227851

Bonne SL, Kadri SS. Evaluation and management of necrotizing soft tissue infections. Infect Dis Clin North Am. 2017;31(3):497–511. https://doi.org/10.1016/j.idc.2017.05.011

Chaudhry AA, Baker KS, Gould ES, Gupta R. Necrotizing fasciitis and its mimics: what radiologists need to know. Am J Roentgenol. 2015;204(1):128–139. https://doi.org/10.2214/AJR.14.12676

Chen KCJ, Klingel M, McLeod S, Mindra S, Ng VK. Presentation and outcomes of necrotizing soft tissue infections. IJGM. 2017;10:215–220. https://doi.org/10.2147/IJGM.S131768

Cheung JP, Fung B, Tang WM, Ip WY. A review of necrotising fasciitis in the extremities. Hong Kong Med J. 2009;15(1):44–52

Das DK, Baker MG, Venugopal K. Risk factors, microbiological findings and outcomes of necrotizing fasciitis in New Zealand: a retrospective chart review. BMC Infect Dis. 2012;12(1):1–8. https://doi.org/10.1186/1471-2334-12-348

Davoudian P, Flint NJ. Necrotizing fasciitis. Contin Educ Anaesth Crit Care Pain. 2012;12(5):245–250. https://doi.org/10.1093/bjaceaccp/mks033

Fernando SM, Tran A, Cheng W et al. Necrotizing soft tissue infection: diagnostic accuracy of physical examination, imaging, and LRINEC score: a systematic review and meta-analysis. Ann Surg. 2019;269(1):58-65. https://doi.org/10.1097/SLA.0000000000002774

Goh T, Goh LG, Ang CH, Wong CH. Early diagnosis of necrotizing fasciitis. Br J Surg. 2014;101(1):e119–e125. https://doi.org/10.1002/bjs.9371

Hasham S, Matteucci P, Stanley PR, Hart NB. Necrotising fasciitis. BMJ. 2005;330(7495):830–833. https://doi.org/10.1136/bmj.330.7495.830

Hung TH, Tsai CC, Tsai CC, Tseng CW, Hsieh YH. Liver cirrhosis as a real risk factor for necrotising fasciitis: a three-year population-based follow-up study. Singapore Med J. 2014;55(7):378-82. https://doi.org/10.11622/smedj.2014090

Hunter J, Quarterman C, Waseem M, Wills A. Diagnosis and management of necrotizing fasciitis. Br J Hosp Med. 2011;72(7):391–395. https://doi.org/10.12968/hmed.2011.72.7.391

Kiat HJ, Natalie YHE, Fatimah L. Necrotizing fasciitis: how reliable are the cutaneous signs? J Emerg Trauma Shock. 2017;10(4):205–210. https://doi.org/10.4103/JETS.JETS_42_17

Krapp F, Morris AR, Ozer EA, Hauser AR. Virulence characteristics of carbapenem-resistant Klebsiella pneumoniae strains from patients with necrotizing skin and soft tissue infections. Sci Rep. 2017 Oct 19;7(1):13533. https://doi.org/10.1038/s41598-017-13524-8

Kückelhaus M, Hirsch T, Lehnhardt M, Daigeler A. Necrotizing fasciitis of the upper and lower extremities. Der Chirurg. Chirurg. 2017;88(4):353–366. https://doi.org/10.1007/s00104-017-0397-0

Lin CN, Hsiao CT, Chang CP et al. The relationship between fluid accumulation in ultrasonography and the diagnosis and prognosis of patients with necrotizing fasciitis. Ultrasound Med Biol. 2019;45(7):1545–1550. https://doi.org/10.1016/j.ultrasmedbio.2019.02.027

Maya SP, Beltrán DD, Lemercier P, Leiva-Salinas C. Necrotizing fasciitis: an urgent diagnosis. Skeletal Radiology. 2014;43(5):577–589. https://doi.org/10.1007/s00256-013-1813-2

Menichetti F, Giuliano S, Fortunato S. Are there any reasons to change our behavior in necrotizing fasciitis with the advent of new antibiotics? Curr Opin Infect Dis. 2017;30(2):172–179. https://doi.org/10.1097/QCO.0000000000000359

Misiakos EP, Bagias G, Patapis P et al. Current concepts in the management of necrotizing fasciitis. Front Surg. 2014;1:36. https://doi.org/10.3389/fsurg.2014.00036

Morgan MS. Diagnosis and management of necrotising fasciitis: a multiparametric approach. Journal of Hospital Infection. 2010;75(4):249–257. https://doi.org/10.1016/j.jhin.2010.01.028

Moues CM, Van den Bemd GJCM, Heule F, Hovius SER. Comparing conventional gauze therapy to vacuum-assisted closure wound therapy: a prospective randomised trial. J Plast Reconstr Aesthetic Surg. 2007;60(6):672–681. https://doi.org/10.1016/j.bjps.2006.01.041

Murphy G, Markeson D, Choa R, Armstrong A. Raised serum lactate: a marker of necrotizing fasciitis? J Plast Reconstr Aesthet Surg. 2013;66(12):1712–1716. https://doi.org/10.1016/j.bjps.2013.07.008

Olsen RJ, Musser JM. Molecular pathogenesis of necrotizing fasciitis. Annu Rev Pathol Mech Dis. 2010;5(1):1–31. https://doi.org/10.1146/annurev-pathol-121808-102135

Peetermans M, de Prost N, Eckmann C et al. Necrotizing skin and soft-tissue infections in the intensive care unit. Clin Microbiol Infect. 2020;26(1):8–17. https://doi.org/10.1016/j.cmi.2019.06.031

Puvanendran R, Huey JCM, Pasupathy S. Necrotizing fasciitis. Can Fam Physician. 2009;55(10):981–987

Rogers S, Commons R, Danchin MH et al. Strain prevalence, rather than innate virulence potential, is the major factor responsible for an increase in serious group A streptococcus infections. J Infect Dis. 2007;195(11):1625–1633. https://doi.org/10.1086/513875

Sarani B, Strong M, Pascual J, Schwab CW Necrotizing fasciitis: current concepts and review of the literature. J Am College Surg. 2009;208(2):279–288. https://doi.org/10.1016/j.jamcollsurg.2008.10.032

Simonart T. Group a beta-haemolytic streptococcal necrotising fasciitis: early diagnosis and clinical features. Dermatology. 2004;208(1):5–9. https://doi.org/10.1159/000075038

Wilson B. Necrotizing fasciitis. Am Surg. 1952;18(4):416–431

Wong CH, Khin LW, Heng KS, Tan KC, Low CO. The LRINEC (Laboratory Risk Indicator for Necrotizing Fasciitis) score: a tool for distinguishing necrotizing fasciitis from other soft tissue infections. Crit Care Med. 2004;32(7):1535–1541. https://doi.org/10.1097/01.ccm.0000129486.35458.7d

Yaşar NF, Uylaş MU, Badak B et al. Can we predict mortality in patients with necrotizing fasciitis using conventional scoring systems? Ulus Travma Acil Cerrahi Derg. 2017;23(5):383–388. https://doi.org/10.5505/tjtes.2016.19940