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# PRACTICE



## EASILY MISSED?

# **Necrotising fasciitis**

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#### What you need to know

Necrotising fasciitis can present with non-specific signs that evolve rapidly over time, with life threatening consequences

Disproportionate pain is a serious sign that warrants urgent surgical referral and intervention

Understanding the epidemiological risk factors, and timely laboratory and imaging assessments can increase confidence in the diagnosis, but necrotising fasciitis remains a clinical diagnosis that can be supported by ongoing reviews from medical and surgical teams

Successful treatment consists of resuscitation, intravenous antibiotics, and immediate referral to surgical care for aggressive debridement

A 36 year old indigenous Australian woman presents to her general practitioner with non-tender swelling on her flank and no other symptoms (including no fevers or chills). Her medical history includes type 2 diabetes mellitus, hypertension, dyslipidaemia, obesity, and chronic kidney disease. She is given oral antibiotics for presumed cellulitis but does not take them. Five days later, she presents to hospital with progressive generalised abdominal pain, soft tissue swelling, and fever. She is treated with broad spectrum antibiotics (meropenem, vancomycin, and clindamycin), fluid resuscitation, and electrolyte replacement. Her abdomen has several focuses of necrosis, generalised tenderness, and soft tissue induration extending to the bilateral subcostal margins (fig 1). She is taken urgently to theatre for aggressive surgical debridement and resuscitation.

## What is necrotising fasciitis?

Necrotising fasciitis is a rare but serious infection of the subcutaneous tissues and fascia of the skin. The condition has an average mortality rate of  $20.6\%^1$  and is a surgical emergency. It can occur anywhere on the body, but most commonly at the perineum (36%), lower extremities (15.2%), postoperative wounds (14.7%), as well as in the abdomen, oral cavity, and neck.<sup>2</sup> Necrotising fasciitis spreads rapidly with little muscle sparing<sup>3</sup> and often leads to sepsis. If not treated promptly, it has

high morbidity and mortality. Prompt diagnosis and surgery are the cornerstones of therapy to reduce mortality. Necrotising fasciitis carries a notable burden of disease, with health costs (including surgical and critical care) averaging A\$64 517 (£32 360, €36 662, \$39 981) per patient (range A\$1025-514 889) in a retrospective Australian study.<sup>4</sup>

## Why is it missed?

Necrotising fasciitis is missed because it is not only rare, but it presents with non-specific signs and symptoms that change over time. The diagnosis is clinical and requires a high index of suspicion and a low threshold for referral to surgical care. Incidence is roughly 0.3-5 per 100 000 in the general population, with rates 10 times higher in indigenous populations.<sup>5</sup> During the past decade, however, incidence has been increasing in the UK to 500 new cases per year.<sup>67</sup>In children, incidence is 0.0729-0.212 per 100 000.<sup>8</sup> Risk factors are described in box 1.

#### Box 1: Risk factors

Trauma, such as surgery, burns, or soft tissue infections, is a common cause of necrotising fasciitis. Other predisposing factors for infection include injecting drug use, immunosuppression, diabetes mellitus, advanced age, peripheral vascular disease, obesity, alcoholism, and malnutrition, all of which probably act by increasing susceptibility to infection, local tissue injury, or both. Diabetes mellitus is the most common pre-existing medical condition.<sup>3</sup>

A retrospective study of 89 patients highlights that 14.6% of those admitted to hospital had a missed diagnosis of necrotising fasciitis, and alternative causes such as cellulitis or abscess had been considered. In this study, survival was adversely affected by advanced age, the presence of two or more associated comorbidities, and a delay of more than 24 hours in getting patients from admission to surgery. A multivariate logistic regression analysis showed that survival declined with a delay of more than 24 hours from admission to surgery as the only independent predictor of mortality with a relative risk 9.4 (p<0.05).<sup>9</sup> Part of the challenge in making the diagnosis comes from the paucity of specific clinical signs to alert the clinician

Correspondence to J Diab jdmisciali@gmail.comThis is one of a series of occasional articles highlighting conditions that may be more common than many doctors realise or may be missed at first presentation. The series advisers are Anthony Harnden, professor of primary care, Department of Primary Care Health Sciences, University of Oxford, and Dr Kevin Barraclough, School of Social and Community Medicine, University of Bristol. To suggest a topic for this series, please email us at practice@bmj.com.

that a patient definitively has necrotising fasciitis. Early signs include local erythema and swelling, myalgias, and abdominal pain, which can mimic other soft tissue infections. In children, viral illnesses are more common and may present with the same non-specific signs and symptoms. Further, in many cases, common systemic signs, such as fever and tachycardia, are initially absent. The timing of onset for the antecedent symptoms can be hours to seven days (mean two days), but once the diagnosis is made, the evolution of signs can be rapid.<sup>10</sup> The classic findings of gas gangrene with crepitus and skin necrosis are relatively late signs, and septic shock has a poor prognosis by this stage. The disease can progress swiftly without specific signs to reflect the underlying pathophysiological process and progression of disease (box 2).<sup>12</sup>

#### Box 2: Pathogenesis of necrotising fasciitis

Necrotising fasciitis can be sub-classified by pathogens with variable presentations: type 1 (polymicrobial) is the most common, type 2 (beta haemolytic *Streptococcus pyogenes*, monomicrobial), type 3 (*Clostridium* species and Gram negative bacteria), and type 4 (fungal).<sup>11</sup>

- The underlying pathogenesis reflects the evolution of clinical signs over time:
   The subcutaneous infection spreads from either a breach in the soft tissue or haematogenous spread causing erythema and swelling mimicking a soft tissue infection
  - The pathogen then spreads along the horizontal planes, with infarction of the nutrient vessels and nerves, leading to induration and disproportionate pain
  - Finally, the infarction leads to oedematous changes in compartments, forming haemorrhagic bullae and then the appearance of gas gangrene

## How is it diagnosed?

#### Clinical

Necrotising fasciitis is a clinical diagnosis with symptoms and signs that change rapidly over time. Patients with the condition often present in the emergency setting with swelling (75%), pain (72.9%), and erythema (66.3%).<sup>3 10</sup> Initially, many patients present without fever, tachycardia, or rigors and may appear to have common soft tissue infections, such as cellulitis.9 The presence of multiple risk factors, including diabetes mellitus and immunosuppression, have been strongly associated with necrotising fasciitis, particularly in the urogenital region (Fournier's gangrene), and warrant early surgical referral.<sup>13</sup> The classic skin changes of cutaneous necrosis and gas gangrene-along with fever, tachycardia, and other signs of septic shock-often occur later, with severe pain preceding their presentation. A retrospective study of 22 patients noted that palpation of apparently unaffected adjacent skin is more painful for patients with necrotising fasciitis compared with clinically affected skin in cellulitis.<sup>14</sup> Despite limited data on sensitivity and specificity for the diagnosis, pain disproportionate to what would be expected in a superficial soft tissue infection remains a surgical hallmark for consideration of necrotising fasciitis and requires prompt surgical referral and evaluation. In the interim, periodic monitoring of the patient should include serial vital signs and serial physical examination, particularly with respect to pain. To achieve diagnostic acuity in the context of classic signs, a high index of suspicion with urgent surgical consultation should be considered early for patients with erythema, haemodynamic instability, and disproportionate pain during palpation of the affected site. In the absence of well documented positive predictive values or relative risk factors for presenting clinical symptoms and physical exam findings, table 1 represents pooled findings from case series of necrotising fasciitis in the literature.3 10 14

#### Investigations

The Laboratory Risk Indicator for Necrotising Fasciitis (LRINEC) scoring system is an adjunct tool that may help to identify patients at high risk for necrotising fasciitis when severe soft tissue infection is suspected.<sup>15</sup> LRINEC uses a numeric score to predict the likelihood of the condition compared with other soft tissue infections based on biochemical results. While LRINEC scores must always be considered in the context of the overall clinical presentation, patients with scores greater than or equal to 6 should be considered to have necrotising fasciitis (93% sensitive, 94% specific).<sup>16</sup> A LRINEC score of 0, however, cannot rule out necrotising fasciitis in a patient with clinical diagnosis of the disease.<sup>17</sup>

If readily available, imaging can support the diagnosis of necrotising fasciitis when the clinical diagnosis is unclear, but it must not delay surgical referral in the context of suspected septic shock or multiple high risk factors. The radiological test of choice is computed tomography. A retrospective case series showed that computed tomography is superior to plain radiography in identifying soft tissue inflammation with or without gas, yielding 100% sensitivity, 98% specificity, 76% positive predictive value, and 100% negative predictive value for necrotising fasciitis.<sup>15</sup> Magnetic resonance imaging also has a high sensitivity, but is often not accessible in the emergency setting.<sup>18</sup> Clinical judgment, serial examinations, and early discussion of suspected cases across multidisciplinary teams are key to confirming diagnosis.

## How is it managed?

Management of necrotising fasciitis requires an integrated multidisciplinary approach across medical and surgical disciplines to deliver immediate resuscitation, intravenous antibiotics, and early surgical referral. The mainstay of treatment is surgical management with aggressive debridement, which should be performed as soon as practically possible after immediate resuscitation.<sup>19</sup> A systematic review and meta-analysis showed that mortality was statistically significantly lower for surgery within 12 hours (19%) after presentation compared with surgical treatment delayed by more than 12 hours (34%) (odds ratio 0.41, 95% confidence interval 0.27 to 0.61, P<0.01).<sup>1</sup> To control infection, vigilant debridement to healthy tissue is necessary after primary surgery, with further surgical exploration after 24-48 hours, and repeated as necessary. In parallel, promptly start broad spectrum antibiotic coverage for Gram positive cocci, facultative anaerobic Gram negative rods, and anaerobes, in consultation with infectious diseases specialists.

#### Case resolution

Our patient's LRINEC score was 8 on admission. Her test results are in table 2.

Culture swabs grew meticillin resistant *Staphylococcus aureus* and group B streptococcus. Three necrotic abscesses in the suprapubic region were identified as the source of infection. Extensive debridement from the initial source extended towards the subcostal margins and deep to the rectus sheath until healthy tissue was identified (fig 1). The patient had multiple debridements and procedures, with a long length of hospital stay before returning home.

#### How patients were involved in this article

The case described in this article is based on a patient who provided consent for the use of images and permission to publish the story.

#### Education into practice

Consider the last time a patient presented with soft tissue infection that may have had suspicious clinical findings. How would you alter your management approach when discussing with medical, surgical, and intensivist disciplines?

#### How this article was made

The article was based on a real case, which prompted an audit of our education and management across disciplines. We conducted an extensive literature search using search terms "necrotising fasciitis" and "soft tissue infections" in databases (PubMed, Embase, Cochrane) to appreciate current findings. Using our own data and the literature, we presented the findings to our team, which included members with extensive experience in medical and surgical disciplines. Our focus was to highlight the take-home message of early surgical referral, with an appreciation of the surgical hallmark of disproportionate pain.

Patient consent obtained.

Provenance and peer review: commissioned, based on an idea from the author; externally peer reviewed.

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- Nawijn F, Smeeing DPJ, Houwert RM, Leenen LPH, Hietbrink F. Time is of the essence when treating necrotizing soft tissue infections: a systematic review and meta-analysis. World J Emerg Surg 2020;15:4. PubMed 10.1186/s13017-019-0286-6
- 2 Elliott DC, Kufera JA, Myers RA. Necrotizing soft tissue infections. Risk factors for mortality and strategies for management. *Ann Surg* 1996;224:672-83. PubMed 10.1097/00000658-199611000-00011
- 3 Wilson B. Necrotizing fasciitis Am Surg 1952;18:416-31.
- 4 Widjaja AB, Tran A, Cleland H, Leung M, Millar I. The hospital costs of treating necrotizing fasciitis. ANZ J Surg 2005;75:1059-64. PubMed 10.1111/j.1445-2197.2005.03622.x

- 5 Bocking N, Matsumoto CL, Loewen K, etal High incidence of invasive group A streptococcal infections in remote indigenous communities in Northwestern Ontario, Canada. Open Forum Infect Dis 2016;4:ofw243. PubMed 10.1093/ofid/ofw243
- 6 Das DK, Baker MG, Venugopal K. Increasing incidence of necrotizing fasciitis in New Zealand: a nationwide study over the period 1990 to 2006. *J Infect* 2011;63:429-33. PubMed 10.1016/j.jinf.2011.07.019
- 7 Hasham S, Matteucci P, Stanley PR, Hart NB. Necrotising fasciitis. BMJ 2005;330:830-3. PubMed 10.1136/bmj.330.7495.830
- 8 Eneli I, Davies HD. Epidemiology and outcome of necrotizing fasciitis in children: an active surveillance study of the Canadian Paediatric Surveillance Program. J Pediatr 2007;151:79-84. PubMed 10.1016/j.jpeds.2007.02.019
- 9 Wong CH, Chang HC, Pasupathy S, Khin LW, Tan JL, Low CO. Necrotizing fasciitis: clinical presentation, microbiology, and determinants of mortality. *J Bone Joint Surg Am* 2003;85:1454-60. PubMed 10.2106/00004623-200308000-00005
- 10 Bisno AL, Cockerill FR3rd, Bermudez CT. The initial outpatient-physician encounter in group A streptococcal necrotizing fasciitis. *Clin Infect Dis* 2000;31:607-8. PubMed 10.1086/313980
- 11 Morgan MS. Diagnosis and management of necrotising fasciitis: a multiparametric approach. J Hosp Infect 2010;75:249-57. PubMed 10.1016/j.jhin.2010.01.028
- 12 Childers BJ, Potyondy LD, Nachreiner R, etal. Necrotizing fasciitis: a fourteen-year retrospective study of 163 consecutive patients *Am Surg* 2002;68:109-16.
- 13 Singh A, Ahmed K, Aydin A, Khan MS, Dasgupta P. Fournier's gangrene. A clinical review. Arch Ital Urol Androl 2016;88:157-64. PubMed 10.4081/aiua.2016.3.157
- 14 Wang YS, Wong CH, Tay YK. Staging of necrotizing fasciitis based on the evolving cutaneous features. Int J Dermatol 2007;46:1036-41. PubMed
- 10.1111/j.1365-4632.2007.03201.x
  Martinez M, Peponis T, Hage A, etal. The role of computed tomography in the diagnosis of necrotizing soft tissue infections. *World J Surg* 2018;42:82-7. PubMed 10.1007/s00268-017-4145-x
- 16 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;32:1535-41. PubMed 10.1097/01.CCM.0000129486.35458.7D
- Wilson MP, Schneir AB. A case of necrotizing fasciitis with a LRINEC score of zero: clinical suspicion should trump scoring systems. *J Emerg Med* 2013;44:928-31. PubMed 10.1016/j.jemermed.2012.09.039
- 18 Zacharias N, Velmahos GC, Salama A, etal. Diagnosis of necrotizing soft tissue infections by computed tomography. Arch Surg 2010;145:452-5. PubMed 10.1001/archsurg.2010.50
- 19 Bilton BD, Zibari GB, McMillan RW, Aultman DF, Dunn G, McDonald JC. Aggressive surgical management of necrotizing fasciitis serves to decrease mortality: a retrospective study. Am Surg 1998;64:397-400.

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## Tables

Table 1  The evolving clinical findings of necrotising fasciitis			
General findings	Early findings	Late findings	
Fevers	Disproportionate pain on palpation of the site	Haemorrhagic bullae or blisters	
Tachycardia	Hypoesthesia at site	Crepitus	
Delirium	Erythema	Gas gangrene	
Tachypnoea	Swelling	Skin necrosis	
Decreased urine output	Warm skin		
Influenza-like symptoms			

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#### Table 2| Test results on admission

Test	Result
Venous pH	7.15
Potassium	2.4 mmol/L
Bicarbonate	19 mmol/L
Glucose	27 mmol/L
White blood cell count	25.4×10 <sup>9</sup> /L (neutrophilia)
Haemoglobin	111 g/L
Sodium	140 mmol/L
Creatine	124 µmol/L

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## Figure



Fig 1 (A) Three necrotic abscesses in the suprapubic region, circumferentially marked as the initial source of infection (arrows). Although the margins show swelling, erythema, and induration, surgical debridement (B) is far more extensive than what the clinical eye can truly appreciate, extending to bilateral subcostal margins, flanks, and mons pubis