PSNet
PATIENT SAFETY NETWORK

Pitfalls in Diagnosing Necrotizing Fasciitis

August 21, 2014
Goh T, Goh LG. Pitfalls in Diagnosing Necrotizing Fasciitis. PSNet [internet]. 2014.
https://psnet.ahrq.gov/web-mm/pitfalls-diagnosing-necrotizing-fasciitis

Case Objectives

- State the epidemiology of necrotizing fasciitis.
- Appreciate the high mortality associated with necrotizing fasciitis.
- Explain the pathophysiology of necrotizing fasciitis.
- Describe the main challenges in the diagnosis of necrotizing fasciitis.
- List steps that can be taken to avoid errors in the diagnosis of necrotizing fasciitis.

The Case

A 49-year-old previously healthy man presented to the emergency department (ED) after falling from his truck at work 3 days before. He had gone to a different ED the day prior with diffuse pain on his left side (the side of his impact) and was given nonsteroidal anti-inflammatory medications and sent home. He presented to this new ED with persistent and worsening left arm, chest, abdomen, and thigh pain.

On physical examination, he was afebrile but tachycardic. He had diffuse, tender ecchymoses involving his left shoulder, upper chest, lateral abdomen, and thigh. Although the ED physicians felt he had simple bruising from the fall, they noted that he was in severe pain requiring intravenous (IV) opiates and that he was unable to independently ambulate. Because of these symptoms, blood tests were obtained and results showed a white blood cell count of 2.8×10^9/L (normal range: 3.5–10.5×10^9/L) and acute renal insufficiency with a creatinine of 1.4 mg/dL (normal range: 0.6–1.2 mg/dL). A computed tomography scan of the abdomen and pelvis showed "induration in the left quadriceps muscle and fluid layering in the abdominal wall." He was seen by the trauma surgical service, who felt the findings were due to diffuse bruising. The patient was admitted to an internal medicine service.

Due to ED crowding, he remained in the ED overnight, receiving only IV fluids and opiates for his pain. Over the course of the night, his pain worsened and he had a persistent tachycardia. Early morning lab results showed a white blood cell count of 1.6×10^9/L, a creatinine of 1.6 mg/dL, a creatine kinase of 2650 U/L (normal range 55–170 U/L) (evidence of muscle breakdown), and a lactate of 6.2 mg/dL (normal range 0.5–2.2 mmol/L) (evidence of tissue hypoxia). He was seen by the internal medicine team mid-morning and

diagnosed with rhabdomyolysis from trauma and acute renal failure. He continued to receive IV fluids. His pain had become so severe that he was switched to hydromorphone hydrochloride, administered through a patient-controlled analgesia pump.

Later that day, the patient had progressive respiratory distress and developed septic shock. He was re-evaluated by the surgical service and felt to have probable necrotizing fasciitis with pyomyositis. He was urgently taken to the operating room, where he required debridement of 7300 cm/sq (an area roughly 2 ft by 4 ft) of skin and soft tissue from his left arm and axilla, anterior chest wall, abdominal wall, thigh, and leg.

After surgery, he was progressively hypotensive despite multiple vasopressors. He developed multi-organ dysfunction and ultimately, after discussions with his family, care was withdrawn and he died peacefully. He underwent autopsy, which showed necrotizing fasciitis with pyomyositis secondary to methicillin-resistant *Staphylococcus aureus*.

The Commentary

Infections of the skin and soft tissues are incredibly common in pediatric and adult medicine. The classic presentation of erythema, warmth, edema, tenderness, and fever may suggest such an infection. However, physicians must also be mindful of other non-infective diseases that can mimic skin and soft tissue infections (SSTIs), including drug eruptions, foreign body reactions, gout, deep vein thrombosis, contact dermatitis, and muscle contusion. SSTIs involve suppurative bacterial or fungal invasion of the epidermis, dermis, or subcutaneous tissues and can range in severity from benign to very serious (as in this case). An expert panel (1) has classified skin infections into four classes of severity to help guide treatment. The classes range from simple cellulitis (class 1) to life-threatening infections such as necrotizing fasciitis (class 4). This case provides an opportunity to focus on necrotizing fasciitis as this diagnosis is often missed or delayed with devastating consequences.

History and Epidemiology

Hippocrates first alluded to a clinical condition of "necrotizing erysipilas" in the 5th century BC as a complication of erysipelas.(2) Since then, there have been numerous terms given to this condition—phagedena gangrenosum (3), hospital gangrene (4), Meleney gangrene (5), and Fournier gangrene.(6) Wilson accurately coined the term *necrotizing fasciitis* in 1952 (7), describing the dominant feature of the disease to be inflammation and necrosis of the subcutaneous fat and deep fascia, with sparing of the muscle, leading to severe systemic toxicity.

Necrotizing fasciitis (NF) is a rare disease. While SSTIs account for up to 14 million outpatient visits in the United States each year (4530 per 100,000) (8), NF has an incidence of only 0.4 per 100,000 adults.(9,10) The incidence of NF progressively increases among patients aged 50 years and older, reaching 12 per 100,000 in patients older than 80.(11) Necrotizing fasciitis generally impacts patients with chronic illnesses; more than half of patients developing NF have pre-existing medical conditions and 35% have at least two.(12) The majority of adults that acquire NF have at least one of the underlying diseases that will increase their susceptibility to infection (Table 1).(13,14) Despite improved recognition, NF continues to be

associated with a high mortality—in the past decade, it is still reported to be between 15% to 45%.(15)

Pathophysiology of Necrotizing Fasciitis

Necrotizing fasciitis is a peculiar condition in which the skin manifestations apparent to the patient or health care provider lag behind the disease progression under the skin. Understanding the pathophysiology enables the clinician to appreciate the insidious progression of NF despite the paucity of skin signs.

Microbial invasion of the subcutaneous tissues occurs either through external trauma (often seen in fishermen who have injuries from marine organisms), direct spread from a perforated viscus, or from a hematogenous source.(16) Necrotizing fasciitis can affect any part of the body, but the extremities and the perineum are most commonly affected. In the initial stage of NF, the signs are nondescript and it may mimic a typical cellulitis. As the infective process progresses, the skin becomes increasingly tense and erythematous with indistinct margins. The local pain is replaced by numbness, which occurs from compression or infarction of the nerves. As the disease process continues, the skin becomes pale, then mottled and purple looking, and finally gangrenous.(17) In cases where gas-forming anaerobes are present, surgical emphysema (air under the skin) can be palpated (often referred to as *crepitus*). A clinical staging of disease progression has been proposed based on cutaneous signs (Table 2).(18) Symptoms may develop over a period of hours to several days. Patients presenting at an advanced stage may show signs of sepsis and systemic shock.

Historically, group A–beta-hemolytic *streptococcus* has been identified as the major cause of this infection. During the last two decades, scientists have reported that the pathogenesis of necrotizing fasciitis is usually polymicrobial (type 1 NF) rather than monomicrobial (type 2 NF).(19-21) Type 1 NF is a slower process that evolves over 2 to 4 days after the initial insult, while type 2 NF tends to more insidious in onset, but once it presents clinically it progresses more rapidly. The patient in this case had NF secondary to methicillin-resistant *Staphylococcus aureus* (MRSA). Although historically this has not been a common cause of NF, community-acquired MRSA causing NF is an emerging clinical entity. Based on this and the increasing incidence of MRSA in all SSTIs, some have recommended empiric antibiotics that treat MRSA.(22)

Challenges in Diagnosis

A high index of suspicion for NF is needed when SSTIs are encountered. In NF, early diagnosis and adequate debridement within 24 hours is the most important factor impacting survival. Patients who receive surgery in the first 24 hours have a mortality rate of 4.2%–6.7%; those whose surgery is delayed more than 24 hours have mortality rates of 23%–75% (23-28), representing an increase of relative risk for death of 9.4 times.(22)

Early diagnosis of NF is notoriously difficult and misdiagnosis is common. In one study, NF was misdiagnosed 71.4% of the time.(15) Most patients were often treated empirically for non-specific sepsis before a diagnosis of NF was made. There are multiple factors that contribute to mis- or delayed diagnosis. First, NF is a rare disease and hence many practitioners may be encountering it for the first time. Second, NF can present at first in a way that is indistinguishable from other common soft tissue infections (as in this case, where it appeared the patient had simple bruising after his fall). Recognition of the "hard signs" (bullae, numbness, crepitus, and skin necrosis) that distinguish NF will help the clinician make the

diagnosis. Unfortunately, such signs are present in only 43% of these patients.(29) Broad-spectrum antibiotics are often given for suspected infection and can mask the severity of the underlying infection. Third, the cutaneous signs of NF usually lag behind the disease pathology; there can be extensive bacterial load and tissue destruction under the skin with very little in the way of cutaneous manifestations. Fourth, systemic signs of NF may not correlate with the cutaneous signs and vice versa; even patients with extensive infection may not be systemically ill. Systemic manifestations of NF are high fever, hypotension, prostration, and multi-organ failure (i.e., sepsis and septic shock). However, one study found that the incidence of fever ranges from 31.9% to 56.3%.(28) The patients that present with the greatest diagnostic challenge are those who present with severe pain but without fever (up to 47.2%) or systemic signs.(15) What further compounds the challenge is that the initial symptoms of NF can be mild right until the patient rapidly deteriorates and sepsis develops, accompanied by shock and collapse.

Strategies to Improve Diagnosis

Given the multiple features that contribute to missed or delayed diagnoses of NF, providers should be aware of specific strategies to prevent missing the diagnosis. First, suspicion may be aroused by something being "not quite right" for a diagnosis of cellulitis. Pain out of proportion to the skin manifestations is the most consistent feature noted at the time of presentation.(30,31) We found a regular review of the patient's condition with a visual pain score (performed every few hours) very helpful in cases of suspected NF. In this case, the patient's severe pain, requiring increasing intravenous (IV) opiates and a patient-controlled analgesia pump, should have been a sign that this was a more serious infection than originally suspected. Rapid progression of infection with migration of the margins of erythema and skin induration despite the use of antibiotics is an important clue in cases of early NF. Clinicians should be aware (and can notify patients and other providers) that this extension can progress over the course of just a few hours. Three other cutaneous features can serve as diagnostic clues to differentiate NF from simple soft tissue infections. First, in NF, the margins of involvement are often indistinct and poorly defined (in contrast to erysipelas). Second, the tenderness extends beyond the apparent involved area. Third, lymphangitis (inflammation of the lymphatics that can be seen as streaking along the skin) is rarely seen in NF as the pathology is in the deep fascia and not in the dermis.(32)

A multiparametric approach suggested by Morgan (14), with clinical acumen as the cornerstone, backed by several tools, such as blood investigations, LRINEC [Laboratory Risk Indicator for Necrotizing Fasciitis] scoring (33), and diagnostic imaging, is crucial to improve the speed and accuracy of diagnosis. Use of clinical pathways (34) and involvement of multidisciplinary teams with updates and education of frontline medical staff will help to promote awareness of NF.

The patient in the illustrative scenario presented with a history of trauma and at first glance, based on the clinical examination and diagnostic tests, this appeared to be a simple bruise. While nonsteroidal anti-inflammatories (NSAIDs) were likely an appropriate initial treatment, it is recognized that NSAIDs may impede the diagnosis of NF.(35) However, over time, this patient did exhibit a cardinal sign in NF—pain out of proportion to the working diagnosis. The need for escalating IV opiates likely should have raised concerns for NF and prompted further diagnostic testing. It seems that the crowded emergency department may have contributed to the delay in diagnosis as well. This stresses the importance of updating the frontline staff and having a high index of suspicion if the patient does not improve.

Take-Home Points

- Early diagnosis of necrotizing fasciitis and early debridement is crucial to patient survival and reduction in morbidity and need for amputation.
- Early presenting signs of necrotizing fasciitis can be non-specific.
- Pain out of proportion to what one would expect for a simple cellulitis should ring alarm bells and prompt the physician to expand the differential diagnosis to include necrotizing fasciitis.
- There is an evolution of clinical signs of necrotizing fasciitis—from early to late stages.
- A keen sense of suspicion and constant review of a patient are the only ways to reliably detect necrotizing fasciitis at an early stage.

Terence Goh, MBBS

Department of Plastic Surgery

Singapore General Hospital

Singapore

Lee Gan Goh, MBBS

Division of Medicine

University Medicine Cluster

National University Health System

Singapore

Faculty Disclosure: *Terence Goh and Lee Gan Goh have declared that neither they, nor any immediate member of their families, have a financial arrangement or other relationship with the manufacturers of any commercial products discussed in this continuing medical education activity. In addition, the commentary does not include information regarding investigational or off-label use of pharmaceutical products or medical devices.*

References

1. Eron LJ, Lipsky BA, Low DE, et al. Managing skin and soft tissue infections: expert panel recommendations on key decision points. J Antimicrob Chemother. 2003;52(suppl 1):i3-i17. [go to PubMed]

2. Descamps V, Aitken J, Lee MG. Hippocrates on necrotising fasciitis. Lancet. 1994;344:556. [go to PubMed]

3. Jackson R, Bell M. Phagedena: gangrenous and necrotic ulcerations of skin and subcutaneous tissue. Can Med Assoc J. 1982;126:363-368. [go to PubMed]

4. Quirk WF Jr, Sternbach G. Joseph Jones: infection with flesh eating bacteria. J Emerg Med. 1996;14:747-753. [go to PubMed]

5. Brewer GE, Meleney FL. Progressive gangrenous infection of the skin and subcutaneous tissues, following operation for acute perforative appendicitis: a study in symbiosis. Ann Surg. 1926;84:438-450. [go to PubMed]

6. Fournier JA. Gangrène foudroyante de la verge. La Semaine Medicale. 1883;3:345-348.

7. Wilson B. Necrotizing fasciitis. Am Surg. 1952;18:416-431. [go to PubMed]

8. Hersh AL, Chambers HF, Maselli JH, Gonzales R. National trends in ambulatory visits and antibiotic prescribing for skin and soft-tissue infections. Arch Intern Med. 2008;168:1585-1591. [go to PubMed]

9. Trent JT, Kirsner RS. Diagnosing necrotizing fasciitis. Adv Skin Wound Care. 2002;15:135-138. [go to PubMed]

10. File TM Jr, Tan JS, DiPersio JR. Group A streptococcal necrotizing fasciitis. Diagnosing and treating the "flesh eating bacteria syndrome." Cleve Clin J Med. 1998;65:241-249. [go to PubMed]

11. Luca-Harari B, Ekelund K, van der Linden M, Staum-Kaltoft M, Hammerum AM, Jasir A. Clinical and epidemiological aspects of invasive *Streptococcus pyogenes* infections in Denmark during 2003 and 2004. J Clin Microbiol. 2008;46:79-86. [go to PubMed]

12. O'Loughlin RE, Roberson A, Cieslak PR, et al; Active Bacterial Core Surveillance Team. The epidemiology of invasive group A streptococcal infection and potential vaccine implications: United States, 2000–2004. Clin Infect Dis. 2007;45:853-862. [go to PubMed]

13. de Tullio D, Rossi C, Bolzon S, Scagliarini L, Occhionorelli S. Necrotizing fasciitis: a surgical emergency. Updates Surg. 2010;62:83-87. [go to PubMed]

14. Morgan MS. Diagnosis and management of necrotizing fasciitis: a multiparametric approach. J Hosp Infect. 2010;75:249-257. [go to PubMed]

15. Goh T, Goh LG, Ang CH, Wong CH. Early diagnosis of necrotizing fasciitis. Br J Surg. 2014;101:e119-e125. [go to PubMed]

16. Salcido RS. Necrotizing fasciitis: reviewing the causes and treatment strategies. Adv Skin Wound Care. 2007;20:288-293. [go to PubMed]

17. Jones J. Investigation upon the nature, causes, and treatment of hospital gangrene, as it prevailed in the confederate armies 1861–65. Cambridge: Riverside Press. In: Hamilton FH, ed. Surgical Memoirs of the War of the Rebellion. New York, NY: Hurd and Houghton for the United States Sanitary Commission; 1871.

18. Wang YS, Wong CH, Tay YK. Staging of necrotizing fasciitis based on the evolving cutaneous features. Int J Dermatol. 2007;46:1036-1041. [go to PubMed]

19. Rouse TM, Malangoni MA, Schulte WJ. Necrotizing fasciitis: a preventable disaster. Surgery. 1982;92:765-770. [go to PubMed]

20. McHenry CR, Piotrowski JJ, Petrinic D, Malangoni MA. Determinants of mortality for necrotizing soft-tissue infections. Ann Surg. 1995;221:558-565. [go to PubMed]

21. Andreasen TJ, Green SD, Childers BJ. Massive infectious soft-tissue injury: diagnosis and management of necrotizing fasciitis and purpura fulminans. Plast Reconstr Surg. 2001;107:1025-1035. [go to PubMed]

22. Miller LG, Perdreau-Remington F, Rieg G, et al. Necrotizing fasciitis caused by community-associated methicillin-resistant *Staphylococcus aureus* in Los Angeles. N Engl J Med. 2005;352:1445-1453. [go to PubMed]

23. 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-A:1454-1460. [go to PubMed]

24. Voros D, Pissiotis C, Georgantas D, Katsaragakis S, Antoniou S, Papadimitriou J. Role of early and extensive surgery in the treatment of severe necrotizing soft tissue infection. Br J Surg. 1993;80:1190-1191. [go to PubMed]

25. 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. [go to PubMed]

26. Kuo YL, Shieh SJ, Chiu HY, Lee JW. Necrotizing fasciitis caused by *Vibrio vulnificus*: epidemiology, clinical findings, treatment and prevention. Eur J Clin Microbiol Infect Dis. 2007;26:785-792. [go to PubMed]

27. Elliott DC, Kufera JA, Myers RA. Necrotizing soft tissue infections. Risk factors for mortality and strategies for management. Ann Surg. 1996;224:672-683. [go to PubMed]

28. Hong YC, Chou MH, Liu EH, et al. The effect of prolonged ED stay on outcome in patients with necrotizing fasciitis. Am J Emerg Med. 2009;27:385-390. [go to PubMed]

29. Chan T, Yaghoubian A, Rosing D, Kaji A, de Virgilio C. Low sensitivity of physical examination findings in necrotizing soft tissue infection is improved with laboratory values: a prospective study. Am J Surg. 2008;196:926-930. [go to PubMed]

30. Green RJ, Dafoe DC, Raffin TA. Necrotizing fasciitis. Chest. 1996;110:219-229. [go to PubMed]

31. Patiño JF, Castro D. Necrotizing lesions of soft tissues: a review. World J Surg. 1991;15:235-239. [go to PubMed]

32. Majeski J, Majeski E. Necrotizing fasciitis: improved survival with early recognition by tissue biopsy and aggressive surgical treatment. South Med J. 1997;90:1065-1068. [go to PubMed]

33. 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;32:1535-1541. [go to PubMed]

34. Schuster L, Nuñez DE. Using clinical pathways to aid in the diagnosis of necrotizing soft tissue infections synthesis of evidence. Worldviews Evid Based Nurs. 2012;9:88-99. [go to PubMed]

35. 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;82:225-235. [go to PubMed]

Tables

Table 1. Common risk factors for necrotizing fasciitis.

1. Hyperreflexia
2. Immune suppression
3. End-stage renal failure
4. Cirrhosis
5. Pulmonary diseases
6. Malignancy
7. Use of injection drugs

Table 2. Evolution of physical signs of necrotizing fasciitis, from early to late stages.(18)

Stage 1 (early)	Stage 2 (intermediate)	Stage 3 (late)
• Warm to palpation • Erythema • Tenderness to palpitation (extending beyond the apparent areas of skin involvement) • Swelling	• Blister or bullae formation (serous fluid) • Skin fluctuance • Skin induration	• Hemorrhagic bullae • Skin anesthesia • Crepitus • Skin necrosis with dusky discoloration progressing to frank gangrene

This project was funded under contract number 75Q80119C00004 from the Agency for Healthcare Research and Quality (AHRQ), U.S. Department of Health and Human Services. The authors are solely responsible for this report's contents, findings, and conclusions, which do not necessarily represent the views of AHRQ. Readers should not interpret any statement in this report as an official position of AHRQ or of the U.S. Department of Health and Human Services. None of the authors has any affiliation or financial involvement that conflicts with the material presented in this report. View AHRQ Disclaimers