THE NORTHERN HOSPITAL

NECROTIZING INFECTION AND GANGRENE

"Richard Coeur de Lion, (The Lionheart)", bronze, 1860, Carlo Marochetti

In the fading daylight of the evening of 26th March 1199, King Richard widely known as Coeur de Lion or the "Lionheart" emerged from his tent, impatient of the slow progress of the siege of the castle of the Viscount of Limogue. The Viscount had treacherously allied himself with the French King Philip Augustus, against the English. There seemed to be a lull in the fighting, and so Richard decided to dispense with the tedium of putting on a full set of armor. Only one Frenchman of the defending garrison of the castle had bravery enough to show his head above the ramparts and in a faintly hilarious gesture of defiance took a potshot at Richard with a crossbow, whilst hiding behind a frying pan as

a shield. Richard could not help laughing and applauded the Frenchman's attempted heroics, but in so doing he was fractionally late in avoiding the bolt which struck him fully in the left shoulder, where it remained deeply lodged. Richard, true to his cognomen, remained cool and unconcerned. He did not wish to alarm his men nor to let on to the enemy that the lucky shot had hit home, and so he calmly strolled back through the ranks to his tent as though nothing had happened. Once in his tent he collapsed, and called for his surgeon. Despite his surgeon's frantic efforts to remove the bolt and tend to the wound, Richard became increasingly unwell over the next few days. Eventually his wound turned gangrenous, and twelve days after he had been shot he died in a delirium of agony.

At this time Richard was winning his war against the French King Philip Augustus who had treacherously invaded his lands both in France and England, whilst Richard had been away on crusade in the Holy Lands. His untimely and needless death was a godsend for Philip. He was subsequently able to regain Normandy and many other English possessions in France, due in large part to the incompetence of Richard's successor, his brother the infamous King John.

Richard's momentary lapse in due diligence cost him his life, indeed it changed the course of history in Western Europe and ultimately the world. Necrotizing infection and gas gangrene may have remarkably few external signs early in the disease process. A strong clue to its diagnosis is pain and systemic disturbance that appears quite out of proportion to the external signs. Once King Richard's wound turned gangrenous there was nothing that Twelfth century medicine could do to save him. We must always maintain due diligence for the first signs of necrotizing infection in our patients, lest they suffer the same fate as the great, Richard Coeur de Lion

Inverted crown and coat of arms of Richard the Lionheart beneath a crossbow, indicating the King's death from this weapon, from a manuscript of the Chronica Majora by Matthew Paris (early 13th century)

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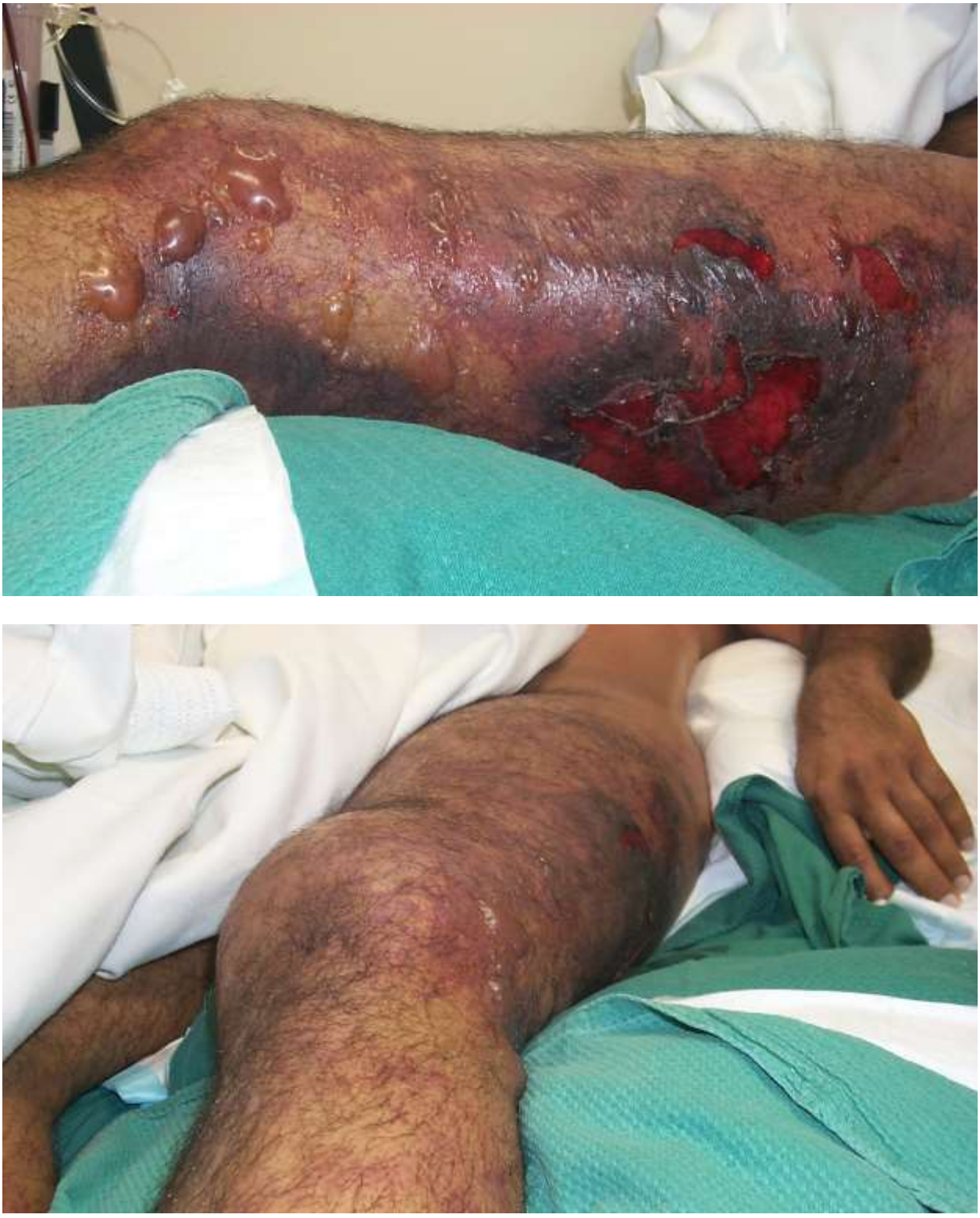


Necrotizing fasciitis and gas gangrene of the thigh in a forty year old male, (Authors, photograph).

Introduction

Necrotizing infections of the skin and soft tissues have a range of clinical manifestations, traditionally given different names, however the pathology of these often overlap and terminology is not precisely defined and hence confusing.

The all encompassing term **rapidly progressive necrotizing infection** is probably the best terminology.

These infections constitute life threatening conditions which require emergent surgical management in addition to antibiotics and supportive care.

Rapidly progressive necrotizing infections of the skin and soft tissues are true life-threatening surgical and medical emergencies.

Untreated the fatality rate of these infections is virtually 100 %.

Even with optimal treatment fatality rates may be as high as 30 %.

Imaging can assist is raising suspicion for necrotizing infections, but surgical exploration is ultimately required for definitive diagnosis.

The most important aspect of management will be surgical debridement of all necrotic tissue.

Terminology

Necrotizing Fasciitis:

Necrotizing Fasciitis is a rapidly progressing necrotizing infection that is primarily confined to the **skin, subcutaneous tissues** and **deep fascia**.

Gas gangrene:

Gas gangrene also known as **clostridial myonecrosis** is a rapidly progressing necrotizing infection that involves the **muscles**.

Gas is produced by gas forming organisms, usually **clostridia.**

The term **"dry gangrene"** is sometimes used for black necrotic tissue that is not infected.

The term **"wet gangrene"** is sometimes used for black necrotic tissue that is infected.

The term **synergistic gangrene** is sometimes used when the infection involves **mixed** aerobe and anaerobe bacterial flora.

Fournier's gangrene:

Fournier's gangrene is simply a term used to describe necrotizing fasciitis that is localized to perineum and genital areas.

History

In the history of Human civilization unnumbered millions of soldiers have died from the complications wounds turned gangrenous.

Perhaps one of the most famous deaths, was that of **Richard the Lionheart**, who was hit by a cross bow bolt in the shoulder. His death saw the momentum of war at that time shift from England to France, with consequences that changed the course of history of Western Europe, and in consequence of that, the course of history of the world.

Pathophysiology

Organisms:

Infecting organisms include: [1]

Mono-microbial:

1 Streptococci

- Especially **Streptococcus pyogenes (i.e group A streptococcus).**

2. Staphylococcus aureus

3. Clostridia:

- **Gas** gangrene is caused by **exotoxin-producing clostridial species** (large, gram-positive, spore-forming bacilli).

  Carbon dioxide and water are the end products of aerobic metabolism.

  Hydrogen, nitrogen, hydrogen sulfide, and methane are produced from the combination of aerobic and anaerobic bacteria in a soft tissue infection. These gases, except carbon dioxide, accumulate in tissues because of reduced water solubility.

  Exotoxin, rather than bacterial proliferation, is responsible for rapid spread of infection in clostridial gas gangrene. Exotoxin causes muscle destruction and creates an anaerobic environment conducive to further bacilli growth.

  Products of tissue breakdown (eg, myoglobin, potassium) can cause secondary toxicity.

- These **anaerobic** organisms normally are found in soil and the gastrointestinal tract.
- **Clostridium perfringens** causes 80-95% of cases of gas gangrene.

  Other clostridial species may include:

  - ♥ *Clostridium novyi*
  - ♥ *Clostridium septicum*
  - ♥ *Clostridium histolyticum*
  - ♥ *Clostridium bifermentans*
  - ♥ *Clostridium fallax*

4. Occasionally some Vibrio species or other water-borne organisms

Polymicrobial:

Synergistic gangrene involves mixed **aerobe** and **anaerobe** bacterial flora.

Most commonly these organisms will include:

- Escherichia coli
- Bacteroides fragilis
- Streptococci
- Staphylococci.

Polymicrobial necrotising infections are most commonly associated with: [2]

- Surgical procedures involving the bowel or penetrating abdominal trauma
- Decubitus ulcers or a perianal abscess
- The site of injection in intravenous drug users
- Spread from a Bartholin abscess or vulvovaginal infection.

Risk Factors:

Predisposing factors for **rapidly progressing necrotizing infections** of the skin and soft tissues include:

1. **Trauma - Penetrating** and **non-penetrating crush injuries**:

- These are particularly likely to cause these rapidly necrotizing skin and soft tissue infections.

- Surgical procedures.

2. Contaminated wounds:

   - Soil contamination

   - Foreign bodies.

   - Intravenous drug abuse.

3. Ischemic wounds:

   - Vascular compromise (including patients with Peripheral vascular disease).

     De-oxygenation necrotic tissue is especially conducive to clostridial infection.

4. Immunocompromise:

   Including:

   - **Diabetes**, malignancies, alcoholism, HIV, the elderly

It should also be noted however that life-threatening *S. pyogenes* necrotizing fasciitis can occasionally occur spontaneously without any apparent precipitating or predisposing factors. [2]

Clinical Features

Classic descriptions distinguish **necrotizing fasciitis,** where infection predominantly affects the subcutaneous tissues and deep fascia, from **gas gangrene** where there is a deeper myonecrosis and earlier systemic toxicity.

In practical terms however the clinical distinction can be difficult and there is often overlap.

It is more useful think of the more general terminology of "**rapidly progressive necrotizing infection**".

Untreated the fatality rate of these infections is virtually 100 %.

Even with optimal treatment fatality rates may be as high as 30 %.

Incubation periods for the development of necrotizing infection is rapid - typically **< 3 days** from the time of a wound.

Spread can then be extremely rapid, advancing as much as **2 cm per hour**

Clinical features suggestive of rapidly progressing necrotizing skin and soft tissue infections include:

1. **Pain** and **tenderness** is **severe** and commonly appears **out of proportion** to the external physical appearance.

2. Local findings may include:

    - Edema, especially extending beyond the margin of erythema.

        ♥ Marked edema can produce a compartment syndrome contributing to myonecrosis and requiring fasciotomy.

    - Inflammatory cellulitic changes.

    - Subcutaneous emphysema (crepitus - i.e "gas gangrene)

    - **Woody (very painful) induration** of the subcutaneous tissue.

    - Foul-smelling or sweet-smelling sero-sanguinous discharge.

    - Ecchymotic areas.

    - Cutaneous anaesthesia

    - Bullae

    - Frankly black necrotic tissue.

5. Systemic findings:

    Progression to toxemia and shock can be rapid especially in cases of clostridial myonecrosis.

    Systemic findings may include:

    - Delirium/ confusion is **common**.

    - Abnormal vital signs:

        ♥ Fever

- ♥ Tachycardia (often out of proportion to the degree of fever)
- ♥ Tachypnea
- ♥ Hypotension, signs of severe sepsis, septic shock, ultimately multiorgan system failure.

Investigations

Blood tests:

1, FBE

2. CRP
   - Very high CRP can be an early indicator of the severity of underlying infection.

3. U&Es/ glucose
   - Renal impairment/ failure
   - Hyperkalemia

4. LFTs

5. CK / myoglobin levels.

6. Coagulation profile.

7. VBGs/ lactate

8. Blood cultures

Plain radiography:

Plain radiography may reveal the presence of gas in subcutaneous fascial planes.

Plain radiography can therefore *suggest* a diagnosis of fasciitis or gas gangrene, but normal radiographs cannot exclude these conditions.

CT scan:

This is an extremely useful imaging modality.

It can more accurately determine the presence of gas along the fascial planes or between muscle bundles as compared to plain radiography.

It can also assess the **extent** and **severity** of infection.

Findings include:

1. Gas in soft tissues

   This is the most useful finding. It is seen most frequently in the setting of clostridial infection or polymicrobial necrotizing fasciitis and is highly specific for necrotizing infections and should prompt urgent surgical intervention.

2. Fluid collections

3. Absence or heterogeneity of tissue enhancement with intravenous contrast

4. Inflammatory changes beneath the fascia.

MRI:

MRI is an alternative imaging option.

Ultrasound:

Ultrasound may also be used for:

1. Detection of localized abscesses

2. Gas in tissues

Its role has however not been well established in necrotizing infections.

Muscle Biopsy and Microbiology:

Surgical exploration will be necessary to definitively establish the diagnosis.

Deep tissue / muscle biopsy is taken for microcopy, gram staining, culture and antibiotic sensitivity studies.

Management

Rapidly progressive necrotizing infections of the skin and soft tissues are true life-threatening surgical and medical emergencies.

Treatment must be aggressive and instituted immediately.

1. Immediate attention to any ABC issues, as clinically indicated.

- Oxygenation
- IV access and fluid resuscitation

2. Analgesia:

   - Most cases will require titrated IV opioid analgesia

3. Antibiotics:

   Urgent empirical antibiotic therapy must be given.

   For empirical therapy for necrotising skin and soft tissue infection use the triad of:[1]

   - **Meropenem 1 gram IV, 8 hourly**

   PLUS

   - **Vancomycin 25 - 30 mg/kg IV as the initial loading dose**

   PLUS

   - **Clindamycin 600 mg IV, 8 hourly.**

   Alternatives:

   - Piperacillin + tazobactam may be used as an alternative to meropenem.
   - Lincomycin may be used as an alternative to clindamycin.

   *Note that **clindamycin (or lincomycin)** is recommended for empirical therapy of necrotising **S. pyogenes** skin and soft tissue infection because of a theoretical reduction in bacterial toxin production; however, clinical evidence is limited. It is not necessary to include benzylpenicillin in the empirical regimen.*

   Water contaminated infections:

   For water contaminated infections **ciprofloxacin** must be added to the above empirical regimen, because Aeromonas isolates often produce carbapenemase enzymes.

   Use:

   - Ciprofloxacin 400 mg IV, 8 hourly.

Therapy is then modified based on the results of Gram stain, culture and susceptibility testing of a surgical deep tissue sample.

Duration of Therapy:

Continue **IV** treatment until:

- Further debridement is no longer necessary
- There has been clinical improvement
- The patient has been afebrile for 48 - 72 hours;

When the above criteria have been met, **oral antibiotic therapy** guided by susceptibility results can be commenced.

Oral therapy is continued until the infection has resolved, but not necessarily until the wound has healed.

4. Intravenous immunoglobulin:

   - It recommend that **intravenous immunoglobulin** also be used if **Streptococcus pyogenes** necrotising fasciitis is suspected

     Streptococcus pyogenes is typically involved with **traumatic injuries (penetrating** or **non-penetrating)**

     Give **2 grams /kg IV**, as a single dose as soon as possible preferably not later than **72 hours**.

5. Tetanus immunoprophylaxis as indicated.

6. Supportive Care:

   - Inotropes, ventilation, renal support, enteral and haematological support all may be required in the very unwell.

7. **Surgery:**

   - **This is the definitive treatment.**

     Early debridement is associated with better outcomes; survival is significantly increased among patients taken to surgery **within 24 hours** after admission compared with those in whom surgery is delayed. Survival is further increased with intervention within **6 hours**.

The basis of treatment is surgical removal of devitalised tissue (which reduces mortality and assists in diagnosis)

Extensive extremity involvement may require amputation.

Because the disease process may continue to involve additional tissue, daily exploration and further debridement may be necessary.

8. Hyperbaric oxygen therapy:

- Hyperbaric oxygen therapy may be used as an *adjunct* to surgical debridement if available.

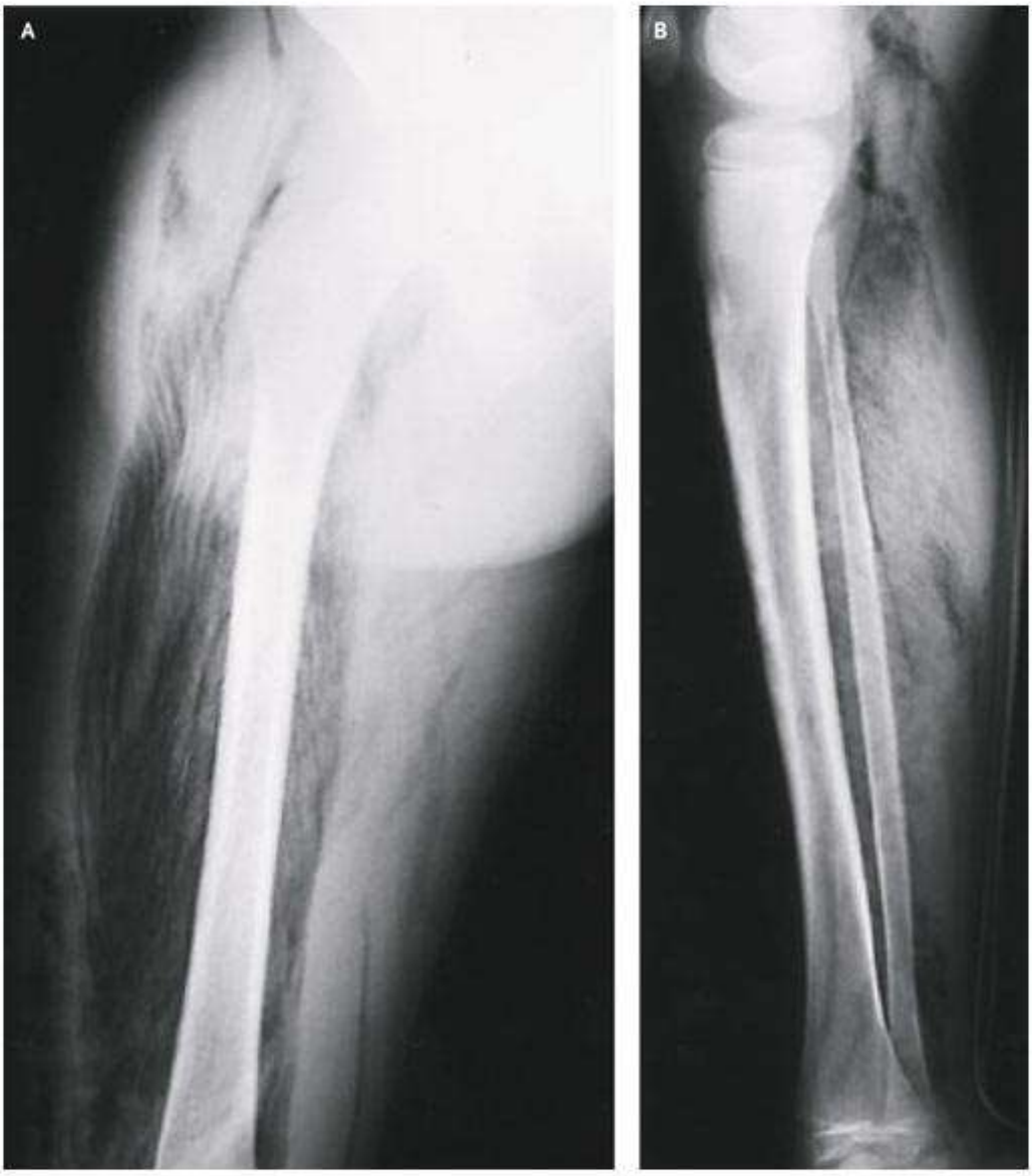
Disposition

Urgent surgical referral

Urgent ID consultation.

All patients with a suspected rapidly progressive necrotizing skin and soft tissue infection should be referred to the **HDU/ ICU**

Appendix 1



Plain radiograph of a tragic case of a 12 year old boy with gas gangrene of the leg. Extensive air can be seen in the subcutaneous tissues, along fascial planes and between major muscle bundles, (NEJM June 2004) [2]

Tomb effigies of King Richard I and his Queen, Berengaria of Navarre, 1199, Fontevraud Abbey, Anjou.

References

1. Necrotizing soft tissue infections - eTG - September 2019

2. Schexnayder S.M, Images in Clinical Medicine, Gas Gangrene, NEJM 17 June, 2004.

3. Dennis L Stevens et al. Necrotizing soft tissue infections in Up to Date Website, August 2019.

Dr J. Hayes
Reviewed September 2019.