Necrotising Fasciitis

Synonyms: necrotising soft tissue infection, Fournier's gangrene (necrotising fasciitis of scrotum or vulva), Ludwig’s angina (necrotising fasciitis of submandibular space)

Necrotising fasciitis (NF) is an uncommon but life-threatening infection. It is defined as necrotising infection involving any layer of the deep soft tissue compartment (dermis, subcutaneous tissue, fascia or muscle).

Be aware that:
- Necrotising fasciitis is difficult to diagnose in its initial stages, as it mimics cellulitis.
- Important early clues are pain, tenderness and systemic illness out of proportion to the localised physical signs.
- Bullae and ecchymotic skin lesions also point to the condition (and are not normally found with cellulitis).
- A high index of suspicion is necessary and suspected cases should be referred immediately. Prompt surgical debridement is essential.

Aetiology and classification

Organisms spread from the subcutaneous tissue along the superficial and deep fascial planes. Muscle is usually spared; however, myonecrosis can occur due to compartment syndrome. Various bacteria may be involved NF infections have been classified into:

- **Type 1 - polymicrobial infection**: with aerobic and anaerobic bacteria; usually in patients with immunocompromise or chronic disease.
- **Type 2 - Group Astreptococcus (GAS)**: occurs in any age group and in otherwise healthy people; occasionally accompanied by staphylococcal infection.
- **Type 3 - Gram-negative monomicrobial infection**:
  - This includes marine organisms such as *Vibrio* spp. and *Aeromonas hydrophila*, which can occur following seawater contamination of wounds, injuries involving fish fins or stings, and raw seafood consumption - particularly in patients with chronic liver disease.
  - These marine infections are particularly virulent and can be fatal within 48 hours.
- **Type 4 - fungal infection**:
  - Zygomyces after traumatic wounds or burns.
  - Candidal infection in immunocompromised patients.
  - Can be rapidly progressive with high mortality.

Epidemiology

- NF is uncommon but carries high mortality and complication rates. Many doctors will encounter at least one case during their career but are unlikely to be familiar with the condition.
- The incidence in the UK is estimated at 500 new cases each year.

Risk factors

These include:
- Skin injury including insect bite, trauma and surgical wounds.
- Underlying conditions including alcohol abuse, intravenous drug abuse, chronic liver or renal disease, diabetes, malignancy, immunosuppression and possibly, tuberculosis.
- NF in children may follow varicella zoster infection.
Note that NF can occur in previously healthy people with no underlying disease, particularly where Group A streptococci are involved.

Presentation[3]

General points
- Have a high index of suspicion for NF - for example, with unexplained limb pain.
- Patients are systemically ill with disproportionately severe pain; there are only minor skin changes in the early phases.
- NF can affect any part of the body but usually involves the extremities, perineum or trunk.
- Ask about recent injury or illness, sea water exposure or fish sting and underlying conditions including intravenous drug abuse.

Symptoms and signs[2, 8, 9, 10]
NF typically develops over a few days but can progress much more rapidly in some cases - eg, with infection with Vibrio spp. and A. hydrophila where it may be fatal within 48 hours. The typical development of symptoms and signs is:

Days 1-2 approximately:
- Local pain, swelling and erythema. This mimics cellulitis or erysipelas: the necrotising infection is deep in the skin and not visible.
- **Severe, constant pain, out of proportion to the physical signs, is a notable feature.**
- The margins of infection are poorly defined, with tenderness extending beyond the apparent area of involvement (unlike cellulitis).
- There is no response to antibiotics (unlike cellulitis).
- Lymphangitis is rarely seen (unlike cellulitis).
- Systemic illness - malaise, tachycardia ± fever and dehydration. One review suggests that patients often ‘feel worse than they have ever felt and don't know why’. [9]

Days 2-4 approximately:
- The area develops tense oedema, extending beyond the margin of erythema.
- There may be bullae, indicating skin ischaemia (unlike cellulitis). These may become haemorrhagic.
- Skin becomes discoloured, progressing to grey necrosed skin which breaks down.
- The subcutaneous tissues have a wooden-hard feel (unlike cellulitis or erysipelas). Fascial planes and muscle groups are not palpable.
- There may be crepitus due to subcutaneous gas.
- Pain sensation may progress from intense tenderness to anaesthesia as the nerves are destroyed.
- There may be a broad erythematous tract in the skin along the route of the infection as it advances cephalad.
- If there is an open wound, probing the edges with a blunt instrument produces easy dissection of the superficial fascial planes well beyond the wound margins.

Days 4-5 approximately:
- Hypotension and septic shock develop.
- Patients become confused and aphatic.

Fournier's gangrene is a rapidly progressive form of infective NF of the perineal, genital or perianal regions, leading to thrombosis of the small subcutaneous vessels and necrosis of the overlying skin. [11]

Differential diagnosis
- Cellulitis or erysipelas.
- Pyoderma gangrenosum.
- Limb ischaemia, compartment syndrome.
- Deep vein thrombosis or thrombophlebitis.
Osteomyelitis with soft tissue involvement.

Diagnosis \cite{2,3}

The diagnosis is clinical - if there is strong clinical suspicion of NF, exploratory surgery is required regardless of test results.

A high index of suspicion is needed when a patient presents with cutaneous infection causing swelling, pain and erythema, particularly if the patient also has diabetes, malignancy, alcohol abuse, or chronic liver or kidney disease. \cite{2} The presence of bullae or gas on plain X-ray can be diagnostic. Early surgical exploration is advised when there is any uncertainty. \cite{12}

During surgery, the diagnosis of NF is made on its macroscopic features, which include: grey necrotic tissue, lack of bleeding, thrombosed vessels, 'dishwater pus', lack of resistance to finger dissection and non-contracting muscle.

Investigations \cite{3}

The following tests may help to identify necrotising infection where the clinical picture is uncertain. However, note that there is no definitive test and surgery is required to confirm or rule out NF.

- Blood tests - may show leukocytosis, acidosis, altered coagulation profile, hypoalbuminaemia and abnormal renal function. \cite{5} (NB: an inflammatory response may be absent in patients who are immunosuppressed or with liver disease.) Pointers to necrotising infection include:
  - White cell count >15.4 x 10^{9}/L.
  - Serum sodium less than 135 mmol/L.
  - Raised CRP ( >16 mg/dL).
  - Raised CK level (>600 U/L).
  - Urea >18 mg/dL.

- Bedside finger test:
  - This is carried out under local anaesthesia, with an incision of 2 cm down to the deep fascia. Gentle probing with the index finger is performed at the level of the deep fascia.
  - Signs of NF are lack of bleeding, malodorous 'dishwater pus' and lack of normal tissue resistance to blunt finger dissection. \cite{13}
  - An alternative is bedside incisional biopsy to the fascia, with immediate frozen section, culture and Gram stain.

- Microbiology:
  - Blood cultures.
  - Wound swab.
  - Gram stain and culture of affected tissues (from surgery or biopsy).
  - Fungal culture is important in the immunocompromised and in trauma patients.

- Radiology - note this cannot rule out NF, as there are many false negatives:
  - Plain X-ray or CT scan may show soft tissue gas.
  - MRI scans may help to show the extent of tissue involvement but may not be accurate and should not delay surgery.
  - Ultrasound has also been used to show subcutaneous gas. \cite{14}

- Other tests:
  - Tissue oxygen saturation measured by near-infrared spectroscopy, as a bedside test. \cite{15}

Management \cite{2,3}

The essential treatment is early and aggressive debridement of the involved tissue. Resuscitation, antibiotics and medical care are also important.
Resuscitation and medical care

- Patients may be shocked or haemodynamically unstable; resuscitation and intravenous fluids may be needed.
- An intensive care unit is often appropriate.

Surgery

Urgent surgical debridement is the key factor in treatment and improved survival of NF. Even a few hours’ delay increases mortality.

- The initial surgery is the most important determinant for survival. The debridement must be extensive, with adequate margins so that no infected tissue remains.
- Following initial debridement, the wound must be observed closely. Surgical debridement is repeated daily until the infection is controlled.
- When the infection is controlled, daily dressings are required under sedation.
- Closure of the wound is by secondary suturing ± skin grafts. Vacuum-assisted wound closing devices may assist healing.\[16, 17]\n
Antibiotics

Immediately start intravenous, broad-spectrum antibiotics at high doses. These should cover streptococci, staphylococci, Gram-negative rods and anaerobes.

Antibiotic regimens for initial treatment of NF

The antibiotic regime will depend on the site of infection, patient allergies and culture results. Examples of recommended regimes include (all drugs given intravenously):

- Benzylpenicillin plus clindamycin plus gentamicin.\[18]\n- If penicillin-allergic, meropenem plus clindamycin plus gentamicin. Review the need for gentamicin daily.\[18]\n- Piperacillin-tazobactam and clindamycin, or benzylpenicillin and clindamycin.\[19]\n
NB:

- Use high, intravenous doses.
- Treatment should be discussed with the local consultant microbiologist and should be adjusted once culture results have returned.
- For suspected *Vibrio* spp. NF, include a tetracycline and third-generation cephalosporin (eg, doxycycline plus ceftazidime); ciprofloxacin may be an alternative.\[2\]

Non-surgical treatment\[20]\n
- Non-surgical measures include close monitoring and general supportive treatment in an intensive care setting with antimicrobial treatment.
- Nutritional support is required from day one, owing to the high protein and fluid loss from the wound (similar to major burns). In severe cases, patients may need twice their basal calorie requirements. Nasogastric feeding may be helpful.
- Broad-spectrum antibiotics such as a benzylpenicillin and flucloxacillin are used.
- Clindamycin has an additional benefit due to its bacteriostatic mechanism. It inhibits the production of the streptococcal superantigen, which greatly contributes to septic shock.

Complications\[2, 3]\n
- NF carries a significant mortality rate, particularly if marine organisms (see 'Aetiology and classification', above) are involved.
- Septic or toxic shock (the latter due to streptococcal endotoxin production).
- The deep tissue infection may lead to vascular occlusion, ischaemia and tissue necrosis. There may be nerve damage and muscle necrosis.
- Large areas of tissue loss may require skin grafting, reconstructive surgery or amputation.
Prognosis

- These infections must be detected and treated rapidly to prevent loss of limb or life.
- One study of NF affecting upper or lower limbs found 22.3% underwent amputation or disarticulation of a limb following failure of multiple debridements to control infection. [21]
- Even with surgery, the mortality rate is 20-40%. [20]
- Increased mortality is associated with delays in diagnosis, poor surgical technique and diabetes.

Prevention

There is controversy regarding prophylaxis for contacts of patients with GAS infection. Guidelines from the Health Protection Agency advise that:

- All contacts should receive information about symptoms of invasive GAS and when to seek medical help.
- Prophylactic antibiotics are advised for:
  - Neonates and their mothers, if either has invasive GAS.
  - Close contacts who have symptoms suggestive of localised GAS - eg, sore throat, fever, skin infection.
  - A household, if two or more cases of invasive GAS disease occur within one month.
- Penicillin V is the first choice for prophylaxis; azithromycin is an alternative.

Further reading & references

- Antibiotic guidelines; Acute Medicine
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