World Journal of Pharmaceutical and Life Sciences
WJPLS
SJIF Impact Factor: 6.129

NECROTIZING FASCIITIS - FLESH EATING BACTERIA SYNDROME

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Article Received on 30/11/2020 **Article Revised on 20/12/2020** **Article Accepted on 10/01/2021**

ABSTRACT

Necrotizing Fasciitis is also called flesh-eating bacteria syndrome. It is an infection that leads to death of components of body's soft tissue present below the skin.[7,1] It is a severe sickness of unforeseen onset that spreads apace. Symptoms embrace red or purple skin within the affected space, severe pain, fever, and unconditioned reflex.[7,2] The foremost normally affected areas are the limbs and region. Typically, the infection enters the body through an opening within the skin like a cut or burn.[7,3] Risk factors embrace poor immune perform like from diabetes or cancer, obesity, alcoholism, intravenous drug use, and peripheral artery disease.[7,4] It's not usually unfold between individuals. The sickness is classed into four sorts, reckoning on the infecting organism. Between fifty five and eightieth percent of cases involve over one kind of bacterium Methicillin-resistant staphylococci aureus (MRSA) is concerned in up to a majority of cases. Medical imaging is useful to substantiate the diagnosis.[7,5] Necrotizing fasciitis is also prevented with correct wound care and handwashing. It's typically treated with surgery to get rid of the infected tissue, and intravenous antibiotics typically, a mix of antibiotics is employed, like benzylpenicillin, clindamycin, vancomycin, and gentamicin.[7,6] Delays in surgery are related to a way higher risk of death. Even with high-quality treatment, the chance of death is between twenty five and thirty five percentage.[7,7]

KEYWORDS: Necrosis, immunocomprised, skin infection, gangrene, cellulitis.

INTRODUCTION

Definition

Necrotising fasciitis could be a terribly serious bacterial infection of the soft tissue and fascia. The microorganism multiply and unharness toxins and enzymes that lead to occlusion within the blood vessels. The result is destruction of the soft tissues and connective tissue.

The main types of necrotising fasciitis are
Type I, Type II, Type III and Other: marine organisms

Type I necrotising fasciitis (Polymicrobial)
Bacteria causing type 1 necrotising fasciitis include Staphylococcus aureus, Haemophilus, Vibrio and several other aerobic and anaerobic strains (Escherichia coli, Bacteroides fragillis). It is usually seen in the elderly or in patients affected with diabetes or other conditions.

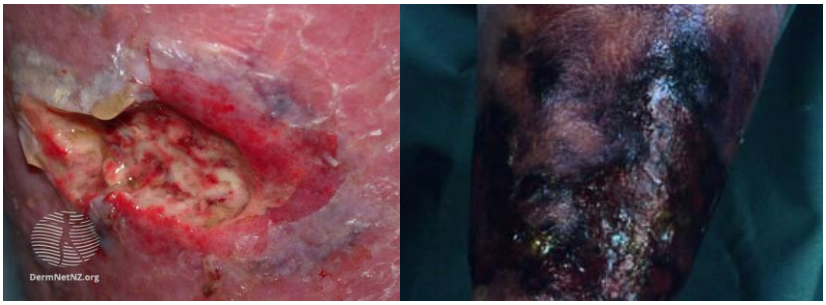
Type II necrotising fasciitis (Due to lysis A eubacteria, staphylococci as well as penicillin resistant strains/ MRSA)
Type II necrotising fasciitis has been sensationalised in the media and is commonly referred to as flesh-eating disease. It affects all age groups. Healthy people are also prone to infection with this group.

Type III necrotising fasciitis (gas gangrene, eg. because of clostridium)
Type III necrotising fasciitis is caused by Clostridia perfringens or less commonly Clostridia septicum. It usually follows significant injury or surgery and results in gas under the skin: this makes a crackling sound called crepitus. IV drug users injecting "black tar" heroin subcutaneously can also be infected with clostridia and develop necrotising fasciitis.

Other Marine Microorganism (vibrio species, Aeromonas hydrophila, type III in some reports) and fungal infections (candida and zygomecetes, type IV in some reports).[2,7.8]

Necrotising fasciitis due to marine organisms is sometimes because of contamination of wounds by sea water, cuts by fish fins or stingers, or consumption of raw seafood. It happens additional usually in patients with liver disorders.[2,7,9,10] These infections may be terribly serious and might be fatal if not attended within

forty eight hours. Fungal necrotising fasciitis complicates traumatic wounds in immunocompromised people. Other terms used for necrotising fasciitis embody haemolytic streptococcal gangrene, Meleney lesion, acute dermal gangrene, hospital gangrene, suppurative fasciitis, and synergistic necrotising cellulitis. Necrotising fasciitis poignant region, venereal and orifice regions is understood as Fournier gangrene. This encompasses a notably high death rate starting from 15% to 50%.[2,7,10,11,12]



Necrotising fasciitis may occur in anyone, in fact, almost half of all known cases of streptococcal necrotising fasciitis have occurred in young and previously healthy individuals. The disease may occur if the right set of conditions is present, these include:

An opening in the skin that allows bacteria to enter the body. This may occur following minor injury (eg small cut, graze, pinprick, injection), or a large wound due to trauma or surgery (eg laparoscopy, sclerotherapy, endoscopic gastrostomy, thoracostomy, caesarean section, hysterectomy). Sometimes no point of entry can be found.[3,6,7,13,14,15]

Cervicofacial necrotising fasciitis can follow mandibular fracture or dental infection.

Direct contact with a person who is carrying the bacteria or the bacteria is already present elsewhere on the person.

Particularly invasive strains of bacteria, eg streptococci that evade the immune system and produce a toxin called cysteine protease SpeB, which dissolves tissue.

In children, type II necrotising fasciitis may complicate chickenpox. Other causes of necrotising fasciitis in chidren include omphalitis, necrotising enterocolitis and urachal anomalies.[4,5,7,16,17,18]

Risk Factors
Aspirin and non-steroidal anti-inflammatory drugs
Advanced age
Diabetes
Immune suppression
Obesity
Drug abuse
Severe chronic illness
Malignancy.[7,19,20,21]

Epidemology: The number of cases reported for necrotizing fasciitis in adults is 0.40 cases per 100,000 people/year while the incidence in children is reportably higher at 0.08 cases per 100,000 people/year. Necrotizing fasciitis is considered a rare condition, however, the mortality rate remains high. Evidence has estimated the mortality rate to be at 20-40%, increasing with the delay in initial diagnosis. According to the Center for Disease Control there is an estimated 9,000-11,500 cases of necrotizing fasciitis occur each year in the United States, with a resultant 1,000-1,800 deaths annually. Although necrotising fasciitis is often fatal in adults, its case fatality rate seems to be lower in children. A highly variable clinical presentation makes the diagnosis challenging, which often results in misdiagnosis and time-delay to therapy.[7,21-30]

Etiology: Surgical procedures may cause local tissue injury and bacterial invasion, resulting in necrotizing fasciitis. These procedures include surgery for intraperitoneal infections and drainage of ischiorectal and perianal abscesses. Intramuscular injections and intravenous infusions may lead to necrotizing fasciitis.

Minor insect bites may set the stage for necrotizing infections. Streptococci introduced into the wounds may be prominent initially, but the bacteriologic pattern changes with hypoxia-induced proliferation of anaerobes.

Local ischemia and hypoxia can occur in patients with systemic illnesses (eg, diabetes). Host defenses can be compromised by underlying systemic diseases favoring the development of these infections. Illnesses such as diabetes or cancer have been described in over 90% of cases of progressive bacterial gangrene.

Of patients with necrotizing fasciitis, 20-40% are diabetic. As many as 80% of Fournier gangrene cases occur in people with diabetes. In some series, as many as 35% of patients were alcoholics. However, approximately one half of the cases of streptococcal necrotizing fasciitis occur in young and previously healthy people.

Liver cirrhosis is an independent risk factor for necrotizing fasciitis.

Studies have shown a possible relationship between the use of nonsteroidal anti-inflammatory agents (NSAIDs), such as ibuprofen, and the development of necrotizing fasciitis during varicella infections. Additional studies are needed to establish whether ibuprofen use has a causal role in the development of necrotizing fasciitis and its complications during varicella infections. This has not previously been described.

Group A beta-hemolytic streptococci have historically been noted as a cause of necrotizing fasciitis, but *Haemophilus aphrophilus* and *S aureus* are also associated with the condition, and some patients have mixed infections involving multiple species of bacteria, including mycobacteria, as well as fungi.[36,37]

A synergistic infection with a facultative anaerobic bacterium may be significant.

PATHOPHYISIOLOGY: Necrotizing fasciitis is characterized by widespread necrosis of the subcutaneous tissue and the fascia. It was once considered an uncommon clinical entity. Although the pathogenesis of necrotizing fasciitis is still open to speculation, the rapid and destructive clinical course of necrotizing fasciitis is thought to be due to multibacterial symbiosis and synergy.[1]

The major cause of infection was found to be group A beta-hemolytic Streptococcus (GABS). This monomicrobial infection is usually associated with an underlying cause, such as diabetes, atherosclerotic vascular disease, or venous insufficiency with edema. GABS usually affects the extremities and mostly the lower extermitis.[1]

During the last 2 decades, researchers have found that necrotizing fasciitis is usually polymicrobial rather than monomicrobial. Anaerobic bacteria are present in most necrotizing soft-tissue infections, usually in combination with aerobic gram-negative organisms. Anaerobic organisms proliferate in an environment of local tissue hypoxia in those patients with trauma, recent surgery, or medical compromise.[1]

Facultative aerobic organisms grow because polymorphonuclear neutrophils (PMNs) exhibit decreased function under hypoxic wound conditions. This growth further lowers the oxidation/reduction potential, enabling more anaerobic proliferation and, thus, accelerating the disease process.

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.

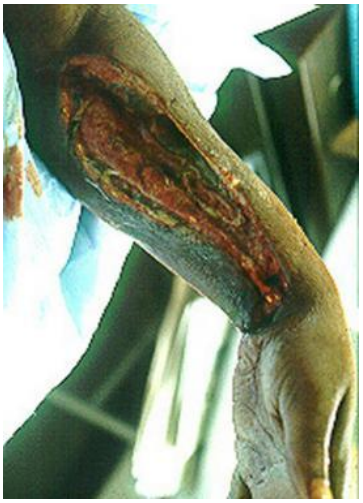
In necrotizing fasciitis, group A hemolytic streptococci and *Staphylococcus aureus*, alone or in synergism, are frequently the initiating infecting bacteria. However, other aerobic and anaerobic pathogens may be present, including the following:

- *Bacteroides*
- *Clostridium*
- *Peptostreptococcus*
- Enterobacteriaceae
- Coliforms (eg, *Escherichia coli*)
- *Proteus*
- *Pseudomonas*
- *Klebsiella*

Bacteroides fragilis is usually noted as part of a mixed flora in combination with *E coli*. *B fragilis* does not directly cause these infections, but it does play a part in reducing interferon production and the phagocytic capacity of macrophages and PMNs.[1,3,4]

A variant synergistic necrotizing cellulitis is considered to be a form of necrotizing fasciitis, it is actually a nonclostridial myonecrosis. This condition begins in the same manner as necrotizing fasciitis, but it progresses rapidly to involve wide areas of deeper tissue and muscle at an earlier stage than might be expected. Severe systemic toxicity occurs.

Anaerobic streptococci, occasionally seen in intravenous drug users, cause many forms of nonclostridial myonecrosis (see the image below). Some cases of necrotizing fasciitis can be caused by *Vibrio vulnificus*. This organism is seen more often in patients with chronic liver dysfunction, and it often follows the consumption of raw seafood. *V vulnificus* may cause subcutaneous bleeding.[7,31]

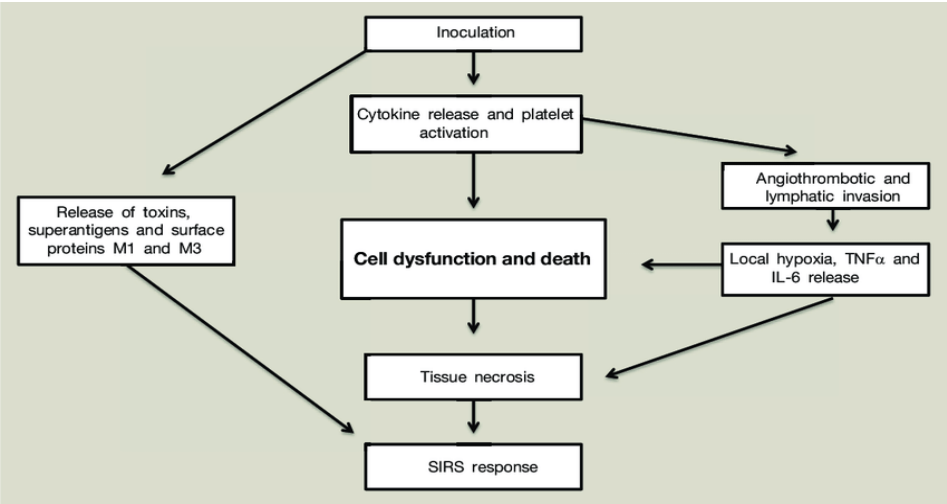


Left upper extremity shows necrotizing fasciitis in an individual who used illicit drugs. Cultures grew Streptococcus milleri and anaerobes (Prevotella species). Patient would grease, or lick, the needle before injection.Organisms spread from the subcutaneous tissue along the superficial and deep fascial planes, presumably

facilitated by bacterial enzymes and toxins. This deep infection causes vascular occlusion, ischemia, and tissue necrosis. Superficial nerves are damaged, producing the characteristic localized anesthesia. Septicemia ensues with systemic toxicity.[7,32]

Important bacterial factors include surface protein expression and toxin production. M-1 and M-3 surface proteins, which increase the adherence of the streptococci to the tissues, also protect the bacteria against phagocytosis by neutrophils.

Streptococcal pyrogenic exotoxins (SPEs) A, B, and C are directly toxic and tend to be produced by strains causing necrotizing fasciitis. These pyrogenic exotoxins, together with streptococcal superantigen (SSA), lead to the release of cytokines and produce clinical signs such as hypotension. The etiological agent may also be a *Staphylococcus aureus* isolate harboring the enterotoxin gene cluster seg, sei, sem, sen, and seo, but lacking all common toxin genes, including Panton-Valentine leukocidin. Community-acquired methicillin-resistant *S aureus* (MRSA) has also been associated with necrotizing fasciitis. Single-nucleotide changes are the most common cause of natural genetic variation among members of the same species. They may alter bacterial virulence; a single-nucleotide mutation in the group A *Streptococcus* genome was identified that is epidemiologically associated with decreased human necrotizing faciitis. It was found that wild-type mtsR function is required for group A *Streptococcus* to cause necrotizing fasciitis in mice and nonhuman primates. It was speculated that a naturally occurring single-nucleotide mutation dramatically alters virulence by dysregulating a multiple gene virulence axis. Severe myositis accompanying septic necrotizing fasciitis may be caused by a Panton-Valentine leukocidin–positive *S aureus* strain. Immunostaining may document strong binding of the Panton-Valentine leukocidin toxin to necrotic muscle tissues.Although necrotizing fasciitis most frequently develops after trauma that compromises skin integrity, it may rarely develop in a healthy person after minor trauma such as an isolated shoulder sprain that occurred without a break in skin barrier.[7,33-40]



SYMPTOMS: The patient may experience fever, blisters, fatigue, pain worse than the wound's apperance.

SKIN: The initial skin changes are similar to cellulitis or abscess, thus making the diagnosis at early stages difficult. Hardening of the skin and soft tissue and swelling beyond the area of skin changes are commonly present in those with early necrotizing changes.The redness and swelling usually blend into surrounding normal tissues. The overlying skin may appear shiny and tense. Other signs which are more suggestive of necrotizing changes are: formation of bullae, bleeding into the skin which is present before skin necrosis, presence of gas in tissues, and reduced or absent sensation over the skin. Rapid progression to shock despite antibiotic therapy is another indication of necrotizing fasciitis. Necrotizing changes affecting the groin are known as Fournier gangrene. However, those who are immunocompromised may not show normal symptoms. Immunocompromised persons also have high risk for mortality.

WHOLE BODY: Fever, chills, hypotension, fatigue.

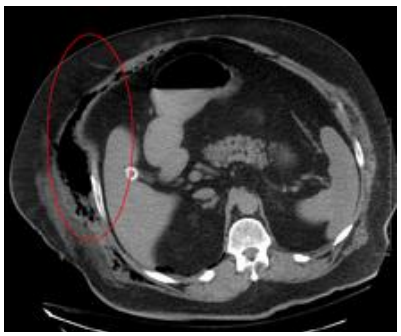
OTHERS: Renal failure, edema, pus.[1,3,5]

DIAGNOSIS: Early diagnosis is difficult, as the disease often looks early on like a simple superficial skIin.When in doubt, a small incision can be made into the affected tissue, and if a finger easily separates the tissue along the fascial plane, the diagnosis is confirmed and an extensive debridement should be performed.

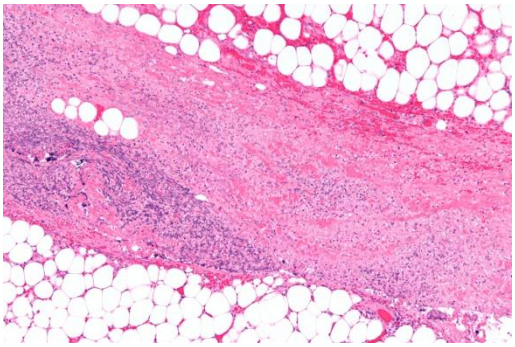
Medical imaging

Imaging has a limited role in the diagnosis of necrotizing fasciitis. The time delay in performing imaging is a major concern. Plain radiography may show subcutaneous emphysema (gas in the subcutaneous tissue), which is strongly suggestive of necrotizing

changes, but it is not sensitive enough to detect all the cases, because necrotizing skin infections caused by bacteria other than clostridial infections usually do not show subcutaneous emphysema. If the diagnosis is still in doubt, computed tomography (CT) scans and magnetic resonance imaging (MRI) are more sensitive modalities than plain radiography. However, both the CT scan and MRI are not sensitive enough to rule out necrotizing changes completely.CT scan may show fascial thickening, edema, subcutaneous gas, and abscess formation.In MRI, when fluid collection with deep fascia involvement occurs, thickening or enhancement with contrast injection, necrotizing fasciitis should be strongly suspected. Meanwhile, ultrasonography can show superficial abscess formation, but is not sensitive enough to diagnose necrotizing fasciitis.



Necrotizing Fasciitis producing gas in soft tissues as shown in CT Scan.



Micrograph of Necrotizing Fasciitis showing necrosis of dense connective Tissue.

Scoring system

A white blood cell count greater than 15,000 cells/mm^3 and serum sodium level less than 135 mmol/l have a sensitivity of 90% in detecting the necrotizing soft tissue infection. It uses six laboratory values: C-reactive protein, total white blood cell count, hemoglobin, sodium, creatinine, and blood glucose.[2] A score of 6 or more indicates that necrotizing fasciitis should be seriously considered. The scoring criteria are:

- CRP (mg/L) ≥150: 4 points
- WBC count (×10^3/mm^3)
  - <15: 0 points
  - 15–25: 1 point
  - >25: 2 points
- Hemoglobin (g/dl)
  - >13.5: 0 points
  - 11–13.5: 1 point
  - <11: 2 points
- Sodium (mmol/l) <135: 2 points
- Creatinine (umol/l) >141: 2 points
- Glucose (mmol/l) >10: 1 point.[4,6]

Differential Diagnosis: This may include Acute Epididymitis, Cellulitis, Orchitis, Emergent Treatment Of Gas Gangrene, Toxic Shock Syndrome.

Treatment

Self Care

Negative-Pressure Wound Therapy: Applying an airtight covering to the wound and then using a vaccum to remove fluid and other material.Done to promote healing.

Surgerical Debridement

It is the process of cutting away the infected area.

Aggressive wound debridement should be performed early, usually as soon as the diagnosis of necrotizing soft tissue infection (NSTI) is made. Surgical incisions often extend beyond the areas of induration (the hardened tissue) to remove the damaged blood vessels that are responsible for the induration. After the wound debridement, adequate dressings should be applied to prevent exposure of bones, tendons, and cartilage so that such structures do not dry out and to promote wound healing.For necrotizing infection of the perineal area (Fournier's gangrene), wound debridement and wound care in this area can be difficult because of the excretory products that often render this area dirty and affect the wound-healing process. Therefore, regular dressing changes with a fecal management system can help to keep the wound at the perineal area clean. Sometimes, colostomy may be necessary to divert the excretory products to keep the wound at the perineal area clean.

Antibiotics

Empiric antibiotics are usually initiated as soon as the diagnosis of NSTI has been made, and then later changed to culture-guided antibiotic therapy. In the case of NSTIs, empiric antibiotics are broad-spectrum, covering gram-positive (including MRSA), gram-negative, and anaerobic bacteria.Moxifloxacin (a fluoroquinolone) and amoxicillin-clavulanate (a penicillin) and evaluated appropriate duration of treatment (varying from 7 to 21 days), no definitive conclusions on the efficacy of treatment, ideal duration of treatment, or the adverse effects could be made due to poor-quality evidence.

Although some necrotizing infections may still be susceptible to penicillin, clindamycin is the treatment of choice for necrotizing infections, for the following reasons:

- Unlike penicillin, the efficacy of clindamycin is not affected by the inoculum size or stage of bacterial growth
- Clindamycin is a potent suppressor of bacterial toxin synthesis
- Subinhibitory concentrations of clindamycin facilitate the phagocytosis of GABS
- Clindamycin reduces the synthesis of penicillin-binding protein, which, in addition to being a target for penicillin, is also an enzyme involved in cell wall synthesis and degradation
- Clindamycin has a longer postantibiotic effect than β-lactins such as penicillin
- Clindamycin suppresses lipopolysaccharide-induced mononuclear synthesis of tumor necrosis factor-α (TNF-α)

Consequently, the success of clindamycin also may be related to its ability to modulate the immune response.
Broad-spectrum beta-lactam drugs such as imipenem cover aerobes, including *Pseudomonas* species. Ampicillin sulbactam also has broad-spectrum coverage, but it does not cover *Pseudomonas* species; however, necrotizing fasciitis caused by *Pseudomonas aeruginosa* is unusual.

If staphylococci or gram-negative rods are involved, vancomycin and other antibiotics to treat gram-negative organisms other than aminoglycosides may be required. The use of vancomycin to treat methicillin-resistant *Staphylococcus aureus* (MRSA) may depend on the clinical situation. For example, use may depend on whether a nasocranial infection is present, or it may need to be avoided in patients who are likely to be carriers of MRSA (eg, those with diabetes, those who use illicit drugs, those undergoing hemodialysis).

Add on therapy

1. **Hyperbaric oxygen**: if available, it helps to reduce mortality.
2. **Intravenous immunoglobulin**, **Fluid and Nutrition supply:** Because of persistent hypotension and diffuse capillary leak, massive amounts of intravenous fluids may be necessary after the patient is admitted to the hospital. Nutritional support is also an integral part of treatment for patients with necrotizing fasciitis. This supplementation should be initiated as soon as hemodynamic stability is achieved. Enteral feeding should be established as soon as possible to offset the catabolism associated with large open wounds.Successful use of intravenous immunoglobulin (IVIG) has been reported in the treatment of streptococcal toxic shock syndrome (STSS).High-dose polyspecific IVIG, along with antimicrobials and a conservative surgical approach is given in patient with group A streptococcal infection patient.
3. **Supportive therapy**: Supportive therapy often including intravenous hydration, wound care, anticoagulants to prevent thromboembolic events, pain control, etc. should always be provided to patients when appropriate.[5,6,7[40-50]]
4. **Prevention:** Take good care of wound and wash your hands regularly. Do not neglect even minor wounds.

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