Necrotizing Soft Tissue Infections: Emerging Bacterial Resistance

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Objectives

- Review definition & diagnostic criteria for NSTI
- Identify the most common bacterial organisms & toxin profile
- Discuss emerging resistance patterns
- Discuss antibiotic management strategies
Necrotizing Soft Tissue Infections (NSTI)

- First described by Jones (1871), US Civil War
  - group A, ß-hemolytic strep. & *Staph aureus*
  - “Hospital gangrene”
- Involvement of the male genitalia described by Fournier (1883)
- “Hemolytic streptococcal gangrene” (Meleney 1924)
- “Necrotizing fasciitis” (Wilson 1952)

**TODAY:** Necrotizing soft tissue infections
- An infection of the soft tissue with associated necrosis requiring operative intervention
- Usually in the context of a critically ill patient
- IVDU, Morbid obesity, emerging resistance
Subcutaneous fat, arteries, veins

Cellulitis

Fasciitis

Myonecrosis

Necrotizing,....

Muscle

Deep fascia

Subcutaneous fat, arteries, veins

Superficial fascia

Dermis

Epidermis

Anatomic layer

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Etiology of NSTI
Elliott, Ann Surg, 1996

- Anal/GU: 42%
- Skin: 11%
- Trauma: 11%
- Diabetic Foot: 12%
- Surgical site: 7%
- IV drug use: 6%
- Pressure ulcer: 2%
- Other: 9%

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Making the diagnosis of NSTI

- Constellation of symptoms, physical signs and laboratory assessment
  - Symptoms
    - Pain out of proportion to physical findings
  - Signs
    - Shock, organ dysfunction if late presentation
    - Local – “hard signs”
    - WBC, Na
  - High risk population?
    - IVDU, Diabetes, obesity

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Hard Signs

- Gas on radiograph

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Tense edema
- Tense edema
- Purple discoloration
- Cutaneous gangrene
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Pannus Infections

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Fournier’s Gangrene, skin changes often an understatement
Delay Associated with Increased Morbidity & Mortality

- UCLA series 2010
  - Debridement >12 hrs after ED arrival
    - Higher mortality
    - Increase in incidence of septic shock
    - Increase in incidence of renal failure
    - Increase in number of debridments required
      - Mean 7.4 vs 2.3

J Trauma epub 2011

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Most common organisms?

- **Monomicrobial infections**
  - Clostridium perfringens (rarely others)
  - Group A streptococci
  - Methicillin resistant staph aureus

- **Polymicrobial infections**
  - All of the above plus gram negative rods and anaerobes

- **Rare but reported**
  - Vibrio vulnificus (exposure to warm sea water)
  - Aeromonas Hydrophilia (warm, brackish fresh water)
Group A streptococcus

- Rapidly progressive, may lead to Toxic Shock Syndrome
- May be seeded from remote pharyngeal infection
- M proteins
  - Filamentous cell membrane protein, antiphagocytic
  - Associated with increased virulence
- Toxins:
  - Pyrogenic exotoxin A,B,C
  - Steptococcal superantigen

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Antimicrobial Coverage for Group A Strep

- High dose Penicillin remains highly effective
- DOSE: 4-6 million units q 4hrs
- Clindamycin recommended for potential anti-toxin effects
- PCN allergy: Vancomycin, Linezolid
Clindamycin for Group A Strep

- Carpetis et al, Clinical Infectious Diseases 2014
  - 84 cases severe GAS infections in Australia
  - Clindamycin treated patients had more severe disease but lower mortality
    - 15% vs 39%
    - Adjusted OR 0.31, 95%CI 0.09-1.12
    - Addition of IVIG appeared to provide additional benefit

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Community Acquired MRSA

- Recent CDC report: 60% of community isolates of staph aureus are methicillin resistant; some communities have reported > 70%
- Majority of these are skin and soft tissue infections
- Panton-Velentine leukocidin gene: more virulent infections
- NSTI due to CA-MRSA have been reported*

* NEJM 325:1145, 2005

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Antimicrobial Coverage for CA-MRSA

- Oral therapy for outpatients: Bactrim, Doxycycline, Fluoroquinolones (moxifloxacin most potent),
  - Avoid Erythromycin (emerging resistance 5-64%)
- IV therapy: Vancomycin, Linezolid, Daptomycin (monitor CPK), Rifampin (synergy only)
- More recent strains with Clindamycin

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Clostridial Infections

- 70-80% *C. Perfringens*, germination time 8 minutes
- Invade and rapidly destroy healthy muscle
- \(\alpha\) toxin (phospholipase C) and \(\theta\) toxin (perfringolysin)
  - Hemolysis, microvascular thrombosis, muscle necrosis
  - Destruction of PMNs and impaired migration
  - Direct inhibition of myocardial contractility
  - Indirect induction of systemic cytokine expression

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Clindamycin

- Excellent first line therapy due to coverage of streptococci, clostridia, and MRSA as well as anaerobic coverage for mixed infections
- High doses recommended to bind toxin & reduce toxin production
  - 900-1200 mg every 6 hours
- 5% of C. perfringens strains are clindamycin resistant thus used in combination with PCN
- Do not use alone for MRSA due to emerging resistance

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Rare but Reported

- Vibrio Vulnificus
  - Exposure of an open wound in warm sea water
  - Doxycycline plus Ceftazidime
- Aeromonas Hydrophilia
  - Exposure to warm fresh water/brackish water
  - Doxycycline plus Cipro or ceftriaxone

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Empiric antimicrobial spectrum should cover streptococci, MRSA, clostridia, and gram negatives

Empiric therapy
- Penicillin 6 million units q4h
  - Strep, clostridium
- Clindamycin 1200 mg q6h
  - Anaerobic coverage (clostridium)
  - Protein synthesis inhibitor – reduces toxin production
- Vancomycin for endemic MRSA
- Gram negative coverage: Fluoroquinolones, gentamicin

Mixed infections (diabetic foot/Fourniers): VANCOMYCIN PLUS: Piperacillin/tazobactam, ertapenem, meropenem, imipenem-cilastin

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IDSA Guidelines, updated 2014
Surgical Management

- Early intervention, prioritize OR availability
- Wide debridement of all necrotic tissue
  - Decompress facial planes
  - May require amputation
- Scheduled return to OR 12 to 24 hours, repeated debridement based on patient condition and progression of necrosis
- Reconstruction: Team Approach

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