Necrotizing Soft Tissue Infections: Delays in Diagnosis

TIME MATTERS!

Eileen M. Bulger, MD
Professor of Surgery
Harborview Medical Center
University of Washington
Disclosure

- Principle investigator for multicenter RCT of AB103, novel immune modulator for NSTI patient
- Previously a consultant for AtoxBio Ltd, Israel for clinical trial design for Phase 3 study
Case

- 27y/o M presents to community hospital with c/o severe pain right shoulder, denies h/o injection drug use
- SBP 120/70 HR 110 T 38.5
- WBC 25K, Na 130, HCT 50, Cr 2.0
- Erythema over deltoid with punctate areas of blue discoloration
- Admitted 3pm on Vancomycin for cellulitis

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Clinical Congress 2015
Next day

- Persistent erythema now extending onto chest wall
- Increased areas of blue discoloration over deltoid and upper back
- WBC 30K
- SBP 90/50 HR 120 after 4 liters crystalloid
Taken to OR

Courtesy of American College of Surgeons Division of Education
Clinical Congress 2015
OR at Community Hospital

- Multiple incisions made to assess the fascia
- NO DEBRIDEMENT
- Call to transfer to tertiary referral center
- Now on vasopressors
Transfer

- Transport via fixed wing aircraft (2hrs)
- Admission labs: wbc 9.5 (84% PMN), Na 132, BUN 91, Cr 3.17, Lactate 2.8, Plt 66
- Wound evaluated and scheduled for emergent debridement
- Started on antibiotics per our NSTI protocol
Post-op: Posterior
Post-op: Anterior

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Post-op course

- Admitted to ICU with ongoing coagulopathy, transfused for post-op anemia
- Post-op labs: wbc 18.4, lactate 6.3 despite aggressive fluid resuscitation
- Levophed and Vasopressin for septic shock
- Returned to the OR 8 hours later: progression of necrosis to intercostal muscle
- Discussions with family led to decision for comfort care and died the evening of 7/31
Objectives

- Challenges in making the Diagnosis
- Impact of Delay in Diagnosis
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
- 4 cases/100,000 population/yr

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Subcutaneous fat, arteries, veins

Cellulitis
Fasciitis
Myonecrosis

Epidermis
Dermis
Superficial fascia
Subcutaneous fat, arteries, veins
Deep fascia
Muscle

Anatomic layer
Necrotizing....
Etiology of NSTI
Elliott, Ann Surg, 1996

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

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Etiology of NSTI
Anaya, Arch Surg, 2004

- Skin 11%
- Ulcer 7%
- Bite 1%
- Other 5%
- Surgical site infection 11%
- Trauma 16%
- Idiopathic 18%
- Anal/GU 1%
- IVDU 30%

Courtesy of American College of Surgeons Division of Education
Clinical Congress 2015
Distribution of Black Tar Heroin

Source: See Table 1. Excepts as noted in Table 1.

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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, immunosuppressed
Hard Signs

- Gas on radiograph
Diabetic foot?
Tense edema
- Tense edema
- Purple discoloration
- Cutaneous gangrene

Courtesy of American College of Surgeons Division of Education
Clinical Congress 2015
Pannus Infections

Courtesy of American College of Surgeons Division of Education
Clinical Congress 2015
SQ Necrosis extends beyond Skin changes
Necrotizing fasciitis (n=31)
 Controls: soft tissue infections without necrosis or not requiring surgical intervention (n=328)
 71% of NSTI due to IV drug use
**“Hard Signs” in NSTI**
Wall, J Am Coll Surg, 2000

<table>
<thead>
<tr>
<th>Condition</th>
<th>NSTI (%)</th>
<th>Non-NSTI (%)</th>
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<tr>
<td>Tense edema</td>
<td>23</td>
<td>3*</td>
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<tr>
<td>Bullae</td>
<td>16</td>
<td>3*</td>
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<tr>
<td>Purplish skin discoloration</td>
<td>10</td>
<td>1*</td>
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<tr>
<td>Sensory/motor deficit</td>
<td>13</td>
<td>3*</td>
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<tr>
<td>Cutaneous necrosis</td>
<td>6</td>
<td>2</td>
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<tr>
<td>Gas on xray</td>
<td>32</td>
<td>3*</td>
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<tr>
<td>Any hard sign</td>
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<td>7</td>
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</tbody>
</table>

*Courtesy of American College of Surgeons Division of Education Clinical Congress 2015*
Predictive model for diagnosis of NSTI
Wall, J Am Coll Surg, 2000

- Best predictors: Admission Na<135 OR WBC>15.4
- Sensitivity: 90%, Specificity: 76%
- Positive predictive value: 26%, Negative predictive value: 99%
- 95% of those without hard signs were predicted to have NSTI using this approach
LRINEC – Laboratory Risk Indicator for NSTI
Wong, Crit Care Med, 2004

- NSTI – 89 patients
- Controls (n=225) - Severe soft tissue infections
  - IV antibiotics >48 hrs OR surgical drainage
- Validated at second institution

Courtesy of American College of Surgeons Division of Education
Clinical Congress 2015
LRINEC for diagnosis of NSTI  
Wong, Crit Care Med, 2004

<table>
<thead>
<tr>
<th>Variable</th>
<th>Score</th>
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<tbody>
<tr>
<td>C-reactive protein</td>
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<td>&lt;150</td>
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<td>&gt;150</td>
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<tr>
<td>WBC</td>
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<td>15-25</td>
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<td>&gt;25</td>
<td>2</td>
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<tr>
<td>Hgb</td>
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<td>&gt;13.5</td>
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<tr>
<td>&lt;11</td>
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<table>
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<tbody>
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<td>Sodium</td>
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<td>≥135</td>
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<tr>
<td>Creatinine</td>
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<tr>
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<tr>
<td>Glucose</td>
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<td>≤180</td>
<td>0</td>
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<tr>
<td>&gt;180</td>
<td>1</td>
</tr>
</tbody>
</table>

Courtesy of American College of Surgeons Division of Education Clinical Congress 2015
LRINEC for diagnosis of NSTI
Wong, Crit Care Med, 2004

- Stratified likelihood of NSTI by LRINEC score
  - Low (≤5): <50%
  - Moderate (6-7): 50-75%
  - High (≥8): >75%

- Using a cutoff of ≥6
  - Positive predictive value: 92%
  - Negative predictive value: 96%
What about imaging?

- Primarily a clinical diagnosis and imaging should not delay surgical intervention.
- Visible gas in the soft tissues is a late finding and not present in the majority of cases.
- CT/MRI: may be useful in identifying deep abscesses when the diagnosis is not clear but fat stranding or fascial thickening is non-specific.

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Are 16-64 slice CT scans better?

- Retrospective review 67 patients who had Contrast CT for possible NSTI
  - Obvious NSTI/ cellulitis excluded
  - Positive scan:
    - Asymmetrical and diffuse areas soft tissue inflammation and ischemia
    - Muscle necrosis
    - Gas across tissue planes
    - Fluid collections
  - Reported sensitivity 100%, Specificity 81%
  - Delay in diagnosis at least one case, not described

Zacharias et al, Arch Surg 2010
MRI?

Yu et al, Emerg Rad 2009

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Clinical Congress 2015
The “Finger Test”?  

- Area infiltrated with local anesthetic
- 2 cm incision down to fascia
  - Lack of bleeding, dishwater fluid ominous
- Push finger along deep fascia – if no resistance, nec fasciitis
Bottom Line

- Need to look at the constellation of risk factors, exam, and lab results
- Making the diagnosis of NSTI requires a high index of suspicion and when in doubt proceed to OR for exploration
Delay in Diagnosis Increases Mortality

- Freischlag et al.
  - Early diagnosis and treatment (< 24hr): 36%
  - Late diagnosis and treatment (>24hr): 70%

- Wong et al.
  - Delay of > 24 hrs from admission to surgery was the only independent predictor of mortality

Wong et al, J Bone Joint Surg Am, 2003

 Courtesy of American College of Surgeons Division of Education Clinical Congress 2015
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

Courtesy of American College of Surgeons Division of Education Clinical Congress 2015
Challenges

- Rare disease
- Limited experience for most surgeons
- Rapidly progressive
- Subtle skin changes
- Shock is a late manifestation

Courtesy of American College of Surgeons Division of Education
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