Module 3: Stewardship in Skin and Soft Tissue Infections

Benjamin Westley MD FIDSA
4120 Laurel St Suite 204
Anchorage, AK 99508
Objectives

- Define classes of uncomplicated skin and soft tissue infection (SSTI) that drive empiric antimicrobial selection
  - Purulent SSTI
  - Non-purulent SSTI

- Recognize conditions that suggest complications are likely and may require alteration of usual empiric regimens

- Identify warning signs and clinical features of necrotizing SSTI

- Discuss classes of Diabetic Foot Infection (DFI) and appropriate initial approaches to therapy

- Brief comment on SSTI in IV drug users (IVDU)
Skin and soft tissue infection

- Multiple terms/categories
  - Cellulitis/erysipelas
  - Impetigo
  - Abscess
  - Skin and soft tissue infection (SSTI)
  - Complicated skin and skin structure infection (cSSSI)
  - Necrotizing fasciitis, Fournier’s gangrene
  - Diabetic foot infection (DFI)

- Used interchangeably, often inappropriately
- Not mutually exclusive
Impetigo

- Superficial crusting/oozing lesions, sometimes bullous
  - MSSA or GAS
  - *RARELY* MRSA

- Single lesions -> Topical mupirocin

- Multiple/recurring lesions -> cephalexin 500mg po qid
Cellulitis

- Red, hot, indurated tender skin
  - Multiple causes, not always infectious
  - Can be non-purulent, or can surround a purulent lesion
- If associated with furuncle, carbuncle, or abscess -> \textit{STAPHYLOCOCCUS AUREUS}
- If diffuse and unassociated with portal of entry -> BETA-HEMOLYTIC STREPTOCOCCI
- Erysipelas = subset of cellulitis
  - Fiery red, tender, painful plaque with well demarcated edges
  - \textit{GROUP A STREPTOCOCCUS}
2014 IDSA SSTI Guidelines

- Categorized SSTI by purulent/non-purulent to guide empiric coverage

- If there is carbuncle/abscess or draining pus = PURULENT*:
  - I+D, send culture on first episode
  - MILD = NO ABX
  - MODERATE = Cellulitis > 5 cm diameter
    - Bactrim DS 1 BID
    - Clindamycin 300mg po TID if Sulfa allergic
  - SEVERE = Purulent SSTI plus SIRS criteria
    - Blood cultures x 2
    - Vancomycin dosed to goal trough of 10-15
    - PO once source controlled and improved to complete 7d Rx

- 5 day duration as effective as 10 days in one study

- Adding cephalexin to trimethoprim/sulfamethoxazole is NOT beneficial

*Cellulitis associated with penetrating trauma or IVDU should be considered “purulent”
Are antibiotics really needed for uncomplicated abscess?

- Data are conflicting.\(^4^{-6}\)
  - 2 prior RCT suggest not
  - NEJM studies published 2016 and 2017\(^25\) suggest small benefit
1265 patients ≥12y old with abscess ≥2cm randomized to TMP/SMX 320/1600 bid vs placebo x7 days

All received I+D with cultures

Average abscess 2.5cm with cellulitis of 6cm

45.3% MRSA

Cure rate higher with ABX than placebo by ~7%
  • ABX 80.5% vs. Placebo 73.6% (P=0.005)

Table 4. Secondary Outcomes in the Per-Protocol Population.*

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Trimethoprim–Sulfamethoxazole</th>
<th>Placebo</th>
<th>Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite clinical cure by test-of-cure visit (%)‡</td>
<td>86.5</td>
<td>74.3</td>
<td>12.2 (7.2 to 17.1)</td>
</tr>
<tr>
<td>Additional surgical drainage procedure (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>By test-of-cure visit</td>
<td>3.4</td>
<td>8.6</td>
<td>-5.2 (-8.2 to -2.2)</td>
</tr>
<tr>
<td>By extended follow-up visit</td>
<td>8.0</td>
<td>13.0</td>
<td>-4.9 (-8.8 to -1.1)</td>
</tr>
<tr>
<td>Hospitalization by test-of-cure visit (%)</td>
<td>3.6</td>
<td>6.4</td>
<td>-2.8 (-5.6 to 0.1)</td>
</tr>
<tr>
<td>Recurrent skin infection at original site (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>By test-of-cure visit</td>
<td>2.1</td>
<td>3.0</td>
<td>-0.9 (-3.0 to 1.2)</td>
</tr>
<tr>
<td>By extended follow-up visit</td>
<td>5.0</td>
<td>4.3</td>
<td>0.7 (-2.1 to 3.4)</td>
</tr>
<tr>
<td>New skin infection at a different site (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>By test-of-cure visit</td>
<td>3.1</td>
<td>10.3</td>
<td>-7.2 (-10.4 to -4.1)</td>
</tr>
<tr>
<td>By extended follow-up visit</td>
<td>10.9</td>
<td>19.1</td>
<td>-8.3 (-12.7 to -3.8)</td>
</tr>
<tr>
<td>Similar infection in household member (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>By test-of-cure visit</td>
<td>1.7</td>
<td>4.1</td>
<td>-2.4 (-4.6 to -0.2)</td>
</tr>
<tr>
<td>By extended follow-up visit</td>
<td>3.8</td>
<td>6.2</td>
<td>-2.4 (-5.2 to 0.4)</td>
</tr>
</tbody>
</table>
Non-purulent cellulitis

- **MILD**
  - Cephalexin or Amoxicillin 1g PO TID

- **MODERATE**
  - Cefazolin 1-2g iv q8h
  - If not improving after 48-72h, broaden to Vancomycin and evaluate for evolution of unrecognized purulent focus

- **SEVERE**
  - Evaluate for necrotizing infection
  - Broad abx
Randomized controlled trial, 524 patients
- Children and adults
- Half (46%) with purulent disease

Bactrim DS BID vs. Clindamycin 300mg TID x 10 days

Equivalent cure rates and complication rates

MODERATE DISEASE
- Excluded T > 38.5°C (adults) and 38.0°C (children)
Clindamycin versus Trimethoprim–Sulfamethoxazole for Uncomplicated Skin Infections
169 patient pre-guideline vs. 175 post-guideline

Interventions:
- Selective CRP, x-ray, blood cx use
- ESR, superficial cultures, CT or MRI imaging DISCOURAGED
- Vancomycin, total Rx IV + PO 7 days
  - Doxycycline, Clindamycin, or Bactrim on discharge
- Broad aerobic GNR or anaerobe coverage DISCOURAGED
- NSAID and elevate legs

Figure 1. Exposure to antimicrobial classes by time period. Broad aerobic gram-negative activity: β-lactam/β-lactamase inhibitor combinations, fluoroquinolones, ceftriaxone, or imipenem-cilastatin. Antipseudomonal activity: piperacillin-tazobactam, ticarcillin-clavulanate, levofloxacin, ciprofloxacin, or imipenem-cilastatin. Broad anaerobic activity: β-lactam/β-lactamase inhibitor combinations, clindamycin, or imipenem-cilastatin. A, All cases; B, patients with cellulitis; C, patients with cutaneous abscess.

Figure 2. Duration of antibiotic therapy by time period. A, All cases; B, patients with cellulitis; C, patients with cutaneous abscess.
Conditions that increase risk of complications

- Periorbital cellulitis
  - Occasionally mixed flora due to sinus-process

- Breast cellulitis
  - May appear non-purulent but often staphylococcal or due to obstructed duct with skin flora and may require surgery

- Parotid or head/neck abscess
  - Staphylococcal and mixed oral flora

- Perirectal/perineal/genital infection
  - Often mixed staphylococcal and GI flora

- Immune compromise
  - Transplant, chemotherapy, immuno-modulatory agents
  - Seek ID input
Necrotizing SSTI¹

- Necrotizing fasciitis
  - Death of tissues along superficial fascial planes

- 2 forms
  - Mono-microbial, usually Group A Strep (Type II)
    - 30 – 80% mortality¹,¹⁰
  - Polymicrobial (GNRs and anaerobes)

- Hallmark features (1 or more)
  - Pain out of proportion to visible lesion
  - Woody subcutaneous tissues rapidly expanding
  - Systemic toxicity (LRINEC score)
  - Crepitus
  - Skin necrosis, ecchymosis, and/or bullous lesions
Fournier’s gangrene

- Subtype of polymicrobial necrotizing fasciitis involving the scrotum/vulva
- Spreads from peri-rectal or perineal lesion
- Enteric mixed flora including clostridium
LRINEC Score

- Laboratory Risk Indicator in Necrotizing Fasciitis
- WBC, Na, glucose, creatinine, and CRP
- Score $>6$
  - 92% PPV
  - 96% NPV
- Score $\geq 6$ in ~90% of patients with necrotizing fasciitis
  - i.e. ~10% with necrotizing fasciitis are <6
- Score $\geq 6$ in 8.4% of patient WITHOUT necrotizing fasciitis
LRINEC scoring

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Score Criteria</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP</td>
<td>&lt;15 mg/dL = 0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>≥15 mg/dL = 4</td>
<td>4</td>
</tr>
<tr>
<td>WBC</td>
<td>&lt;15 x 10³ /uL = 0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>15 – 25 x 10³ /uL = 1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>&gt;25 x 10³ /uL = 2</td>
<td>2</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>&gt;13.5 g/dL = 0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>11 – 13.5 g/dL = 1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>&lt;11 g/dL = 2</td>
<td>2</td>
</tr>
<tr>
<td>Sodium</td>
<td>≥135 mmol/L = 0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>&lt;135 mmol/L = 2</td>
<td>2</td>
</tr>
<tr>
<td>Creatinine</td>
<td>≤1.6 mg/dL = 0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>&gt;1.6 mg/dL = 2</td>
<td>2</td>
</tr>
<tr>
<td>Glucose</td>
<td>≤180 mg/dL = 0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>&gt;180 mg/dL = 1</td>
<td>1</td>
</tr>
</tbody>
</table>
Imaging in necrotizing fasciitis

- CT and/or MRI may show fluid along fascial planes, fascial enhancement, or gas in tissues\textsuperscript{20,21}

- Sensitivity and specificity are poor

- Imaging studies tend to delay surgery

- Clinical impression should drive surgical decision making
  - Small incisions in area of concern made; if no fascial sloughing, necrosis or dehiscence, extensive debridement is not required
Necrotizing Fasciitis ABX

- Vancomycin dosed to goal trough 10-15, PLUS
- Piperacillin/tazobactam per local dosing protocol*, PLUS
- Clindamycin 900mg iv q8h

AND

Immediate surgical consultation!!! It is NOT appropriate to give the above abx for presumed necrotizing infection WITHOUT emergent surgical evaluation

*3.375g iv q8h if extended infusion, 3.375g iv q6h if traditional dosing
Cefepime may be used in place of piperacillin/tazobactam
Clindamycin and Group A Strep

- Clindamycin decreases in-vitro streptococcal toxic shock toxin production and improves animal survival\textsuperscript{12,13}

- Observational data suggests clindamycin decreases mortality in proven severe Group A Streptococcal infections\textsuperscript{8-10,14,17}

- Use WITH a beta-lactam until clinically improved then stop clindamycin and continue beta-lactam
  - E.g. cefazolin 1-2g iv q8h then amoxicillin 1g po TID

- We generally finish therapy with ~10d total Rx but duration should be based on clinical response
IV immune globulin

- Suggestion of mortality benefit in severe group A strep infection with the toxic shock syndrome
  - Multi-organ system dysfunction
  - Shock
  - Often, diffuse erythematous sunburn-like rash and dramatic conjunctival injection

- Data is limited\textsuperscript{10,14-16} and conflicting\textsuperscript{23}

- Dosing not well defined
  - Usually 1 g/kg on day 1 then 0.5 g/kg on days 2 and 3
Diabetic Foot Infection (DFI)

- Updated IDSA guideline in 2012\(^{18}\)
- Not all diabetic ulcers are infected!!
- Signs of infection
  - Redness, warmth, tenderness, pain, induration, or purulent secretions
- MILD
  - Redness ≤ 2 cm around ulcer
- MODERATE
  - Redness >2 cm around ulcer OR deep structures involved
  - WITHOUT sepsis
- SEVERE
  - Local infection plus SIRS criteria
Diabetic Foot Infection

- Infected wounds in NON-SEPTIC patients should be cultured BEFORE antibiotics are started.
- Cultures should be sent from deep tissue by biopsy or curettage AFTER wound is cleaned and superficial tissues debrided.
- All should get plain x-ray.
- MRI if x-ray negative and suspicion of osteomyelitis.
- If wound probes to bone, patient has osteomyelitis.
ABX for DFI$^{18}$

- **MILD to MODERATE severity**
  - Target aerobic GPC only
  - Mild = Cephalexin pending cultures
  - Moderate = Vancomycin dosed to goal trough of 10-15

- **SEVERE**
  - Vancomycin PLUS piperacillin/tazobactam
  - Urgent surgical consultation

- **Duration**
  - Mild: 1 – 2 weeks
  - Moderate – severe: 2 – 3 weeks
  - Osteomyelitis present and not resected: 4+ weeks
  - Osteomyelitis fully resected: 2 – 5 days
DFI Treatment Failure/Recurrence

- Usually due to inadequate offloading, vascular supply, or resection of poorly-viable tissues
SSTI in IV Drug Users

- Increasing frequency in Alaska
- Many users lick either needles and/or injection sites
- Usual presentations:
  - Antecubital fossa abscess
  - Cellulitis with phlebitis
  - Necrotizing fasciitis\(^2\)
- Flora are the usual gram positives including MRSA PLUS oral flora\(^{19,22}\)
  - Streptococcus anginosus group
  - Haemophilus/Eikenella
  - Prevotella/Fusobacterium
- Literature suggests use Vancomycin monotherapy\(^1,19\)
  - We often add ampicillin/sulbactam for severe SSTI in IVDUs
SSTI in IVDU

- Consider instructing patients about safe injection techniques
  - Use chlorhexidine
  - Don’t touch site
  - Don’t lick site or needles
  - Don’t re-use/share needles
- Make sure they were screened for HIV and HCV
- If using heroin, should be given a naloxone rescue kit
References

22. Clinical Infectious Diseases 2001; 33:6–15
23. Clinical Infectious Diseases 2017 Apr 1;64(7):877-885