Update in Management of Skin and Soft Tissue Infections

Catherine Liu, MD
Associate Professor
UCSF, Division of Infectious Diseases

Overview

- Purulent SSTI (abscesses)
- Non-purulent SSTI (cellulitis)
- Recurrent SSTIs
- Necrotizing SSTI
- Potpourri of cases

Disclosures

- None
**Case 1**

32 y/o M with 3 days of an enlarging, painful lesion on his L thigh that he attributes to a "spider bite"

T 36.9 BP 118/70 P 82

**How would you manage this patient?**

A. Incision and drainage alone

B. Incision and drainage plus cephalexin

C. Incision and drainage plus TMP-SMX

D. TMP-SMX alone
IDSA Guideline Recommendations

• MRSA Guidelines (2011)
  — For a cutaneous abscess, I&D is the primary treatment. For simple abscesses or both, I&D alone is likely to be adequate, but additional data are needed to further define the role of antibiotics, if any, in this setting (AII)
  — Antibiotic Rx is recommended for abscesses associated with: severe/extensive disease, signs/sx of systemic illness, associated comorbidities, immunosuppression, extremes of age, abscess in area difficult to drain, associated septic phlebitis, lack of response to I&D alone (AIII)

• Skin and Soft Tissue Infection Guidelines (2014)
  — The decision to administer antibiotics in addition to I&D should be based on presence/absence of SIRS and pts with severely impaired host defenses (strong, low)
  — The addition of systemic antibiotics to I&D of cutaneous abscesses does not improve cure rates, even in those due to MRSA

Results from NIH Trials: Antibiotics + I&D vs. I&D alone

Secondary Outcomes: NIH trials

• Chambers: Recurrence Rates after 1 month:
  — Clinda (7%) vs TMP/SMX (14%) vs placebo (12%)

• Talan: Complications
**NEJM Poll Results: Should Patient be Rx with I&D alone or I&D + TMP-SMX?**

(N=767)

- Case: 22 yo F p/w 2 cm abscess on L thigh. Afebrile, VSS, no other systemic symptoms.
- Exam: 2 cm area of fluctuance with 2 cm area of surrounding erythema

**Should We Change Clinical Practice?**

- **Summary:**
  - Cure rates among pts receiving I&D alone are high
  - Very low risk of serious, invasive infections
  - Abx provide a modest benefit (~10%) over I&D alone

- **Recommendations:** Shared decision-making approach with patients
  - Risks vs benefits

**Microbiology of Purulent SSTIs**

- MRSA 59%
- MSSA 17%
- Other 8%
- Non-hemolytic strep 3%
- Unknown 9%
- Non-hemolytic strep 4%
Empiric PO Antibiotics for Purulent SSTIs (MRSA active agents)

<table>
<thead>
<tr>
<th>PO agents</th>
<th>Dosing</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>TMP-SMX</td>
<td>+/- Q12h</td>
<td>HyperK⁺</td>
</tr>
<tr>
<td>Doxy/mino</td>
<td>+/- Q12h</td>
<td>GI; Photosensitivity</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>++ Q8h</td>
<td>Diarrhea, ↑ resistance</td>
</tr>
<tr>
<td>Linezolid</td>
<td>++ Q12h</td>
<td>$$$; Tox - heme, SSRI</td>
</tr>
<tr>
<td>Tedizolid</td>
<td>++ QD</td>
<td>$$$; better safety profile vs linezolid</td>
</tr>
</tbody>
</table>

1. IDSA guidelines says 1 or 2
2. Prospective study compared 1 vs. 2 tab BID
   • No difference in cure rate: 73% vs. 75% (P=0.79)
3. Recent NIH studies
   • Chambers (1 DS BID) – 93% cure rate
   • Talan (2 DS BID) – 93% cure rate
4. Risk factors for SSTI treatment failure:
   • Retrospective study -- Weight > 100 kg Rx 1 DS BID

**Summary:** 1 DS BID ok, consider 2 DS BID in obese


FDA Approved Agents for Treatment of Complicated SSTI

<table>
<thead>
<tr>
<th>Agent</th>
<th>Dose</th>
<th>Duration</th>
<th>Cost/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vancomycin</td>
<td>15-20 mg/kg q8-12h</td>
<td>7-14 days</td>
<td>$18</td>
</tr>
<tr>
<td>Daptomycin</td>
<td>4 mg/kg q24h, push</td>
<td>7-14 days</td>
<td>$350</td>
</tr>
<tr>
<td>Linezolid PO/IV</td>
<td>600 mg q12h</td>
<td>10-14 days</td>
<td>$280</td>
</tr>
<tr>
<td>Telavancin IV</td>
<td>10 mg/kg q24h</td>
<td>7-14 days</td>
<td>$310</td>
</tr>
<tr>
<td>Ceftaroline IV</td>
<td>600 mg q12h</td>
<td>5-14 days</td>
<td>$250</td>
</tr>
<tr>
<td>Tedizolid PO/IV</td>
<td>200 mg</td>
<td>6 days</td>
<td>$235</td>
</tr>
<tr>
<td>Oritavancin IV</td>
<td>1200 mg once over 3h</td>
<td>1 day</td>
<td>$2900</td>
</tr>
<tr>
<td>Dalbavancin IV</td>
<td>1000 mg x1, 500 mg x1 once/week later over 30 min</td>
<td>8 days</td>
<td>$3000/ $1500</td>
</tr>
</tbody>
</table>

Microbiology of SSTI: Hospitalized Patients

- S. aureus: 97%
- MRSA: 74%
- Streptococci: 7%
- Gram neg: 3%
- Anaerobes: 2%

Slide courtesy of Chip Chambers, M.D.
Antibiotic Utilization Among Hospitalized Patients with SSTI:

- Baseline: N=169

Antibiotic Utilization Among Hospitalized Patients with SSTI: Post-QI Intervention

- Recommended empiric vanco
- Discouraged gram neg/anaerobic
- Suggested Rx for 7 days

Other Outcomes

- Median duration of Rx (13 vs. 10d, p<.001)
- No differences in clinical outcomes
  - Clinical failure (7.7% vs. 7.4%, p=NS)
  - Recurrent infection
  - Rehospitalization due to SSTI
  - Length of hospital stay
- Take home: Gram negative and anaerobic coverage unnecessary in most cases.
  - Exceptions: perirectal/peri orbital infections, critically ill pts with necrotizing SSTI, severe immunocompromise (malignancy on chemotherapy, neutropenia), animal bites, water exposure, severe diabetic foot

IDSA Guidelines on SSTI. 2014
Case 2

28 y/o woman presents with erythema of her left foot over past 48 hrs
No purulent drainage, exudate, or fluctuance.
T 37.0 BP 132/70 P 78

How would you manage this patient?
A. Clindamycin 300 mg TID
B. Cephalexin 500 mg QID
C. Cephalexin 500 mg QID + TMP/SMX 1 DS BID

Nonpurulent Cellulitis: pathogen?

$b$-hemolytic strep vs. $S$. aureus?

- Prospective study, hospitalized patients (N=248)

  Methods
  - Acute and convalescent t/ers (ASO and anti-DNaseB)
  - Rx with $\beta$-lactam antibiotics (cefa/zolin/oxacillin)

  Results
  - 73% due to $b$-hemolytic strep; 27% none identified
  - 96% response rate to $\beta$-lactam antibiotic

- Prospective study, hospitalized patients (N=216)
  - Similar methods as above; 72% due to BHS; 13% probable BHS

Cephalaxin vs. Cephalaxin + TMP-SMX in patients with Uncomplicated Cellulitis

- Cure
- Progression to abscess
- Adverse Events

- Cephalaxin 82.0%
- Cephalaxin + TMP-SMX 81.0%
- Cephalaxin 6.8%
- Cephalaxin + TMP-SMX 6.3%
- 53.0% 49.0%

Eels SJ et al Epidemiology and Infection 2010
What about TMP-SMX for Uncomplicated Cellulitis?

• Multicenter RCT (n=524) of adult/ peds outpts with abscess, cellulitis or both
  – Mean age 27, excluded significant comorbidities
  – Cure rates: TMP-SMX (78%) vs clindamycin (80%)

• Nonpurulent cellulitis subgroup (n=280)
  – Cure rates: TMP-SMX (76%) vs clindamycin (81%)

Summary: TMP-SMX is an option for nonpurulent, uncomplicated cellulitis for younger pts without significant comorbidities.

How Long to Treat?

• Uncomplicated SSTI:
  – 5 days, extend if infection has not improved within this time period

• Complicated SSTI
  – 7-14 days, individualize duration based on clinical response

Case 3

• Patient presents with 4th abscess in 4 months
• Prior abscesses have involved different locations and have been treated with I&D and antibiotics with resolution
• He asks if there is anything he can do to prevent recurrences
How would you manage this patient?

A. Emphasize personal hygiene measures
B. Decolonize with mupirocin and chlorhexidine
C. Decolonize with TMP-SMX and rifampin
D. A and B
E. A and C

How to Manage Recurrent Skin and Soft Tissue Infections?

- Intranasal mupirocin: + data in MSSA SSTI w/ + nasal Cx, no benefit among MRSA colonized military personnel
- Chlorhexidine washes alone: not effective
- Mupirocin + CHG: Household >> individual decol
- Bleach baths: no benefit vs hygiene education
- Oral antibiotics: Mup + hexachlorophene + TMP-SMX or doxy x 10 d ↓ recurrent MRSA SSTI (31 pts); Anecdotal experience with rifampin-based therapy

Combination therapy?

Mupirocin vs. mupirocin + chlorhexidine vs. mupirocin + bleach bath

- Control
- Mup
- Mup+Chlor
- Mup+Bleach

% of patients

Colon. Clear 4m Repeat SSTI 6m p< .02

(Hygiene education alone)
**Recurrent SSTI among Cases and Household Contacts**

(Mupirocin plus chlorhexidine)

<table>
<thead>
<tr>
<th>SSTI 1 mo</th>
<th>SSTI 3 mo</th>
<th>SSTI 6 mo</th>
<th>SSTI 12 mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individual</td>
<td>0%</td>
<td>20%</td>
<td>40%</td>
</tr>
<tr>
<td>Household</td>
<td>0%</td>
<td>20%</td>
<td>40%</td>
</tr>
</tbody>
</table>

*p=0.12, p=0.02, p=0.008, p=0.02*

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**PCN for Prevention of Recurrent Cellulitis**

- Blinded, RCT 274 pts with recurrent cellulitis
  - Penicillin 250 mg BID vs. placebo x 12 months
- Patient characteristics:
  - Edema (66%), venous stasis (25%), tinea pedis (36%)
- Outcomes:
  - Recurrence: 22% (PCN) vs. 37% (placebo), *p=0.01*
  - After treatment stopped, no difference

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**IDSA Guideline Summary Recommendations: Recurrent SSTI**

- **Recurrent Abscesses:**
  - Mupirocin + daily CHG baths and daily decontamination of personal items (towels, sheets, clothes) x 5 days *(weak, low)*

- **Recurrent Cellulitis:**
  - Treat predisposing/underlying conditions *(strong, moderate)*
  - Prophylactic PO penicillin 250 BID or IM benzathine PCN Q 2-4wks *(weak, moderate)*

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**Case 4**

- 39 yo M IVDU with L leg pain and erythema, worsening pain and swelling x 48 hours
  - T 39.2 P 120 BP 90/60 R22 94%RA
  - 18>38<90, Cr 2.4
What would your **empiric** therapy be in this case?

A. Vancomycin and piperacillin-tazobactam
B. Vancomycin and piperacillin-tazobactam, and clindamycin
C. Call surgery, vancomycin and clindamycin
D. Call surgery, vancomycin, piperacillin-tazobactam, clindamycin

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Necrotizing skin and soft infections

- **Monomicrobial**: Group A strep > S. aureus, *Clostridia*, gram neg (*V. vulnificus*, *A. hydrophila*) rare
- **Polymicrobial**: gram +, gram -, anaerobes — associated w/ perianal abscesses, abdominal trauma/ surgery, decubitus ulcers, IVDU, spread from GU tract

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Risk Factors for Necrotizing SSTI

- IVDU
- Diabetes
- Obesity
- Chronic immunosuppression
- Often no precipitating factor

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Why is early diagnosis so important?

*Wong Cll. Jour of Bone and Joint Surg. 2003*

*Mortality rate > 30%*
Necrotizing soft tissue infections: physical findings on admission

Wong CH. Jour of Bone and Joint Surg. 2003

Late findings

n=89; 14% dx with nec fasc on admittance

Necrotizing soft tissue infections: radiographic techniques

- Plain films
  - Low sensitivity
  - Helpful if gas present
- CT and ultrasound
  - May identify other Dx (abscess)
- MRI
  - Enhanced sensitivity, low specificity

Special consideration for the treatment of invasive Group A strep?

- Protein synthesis inhibitors (clindamycin)
  - Decrease toxin production
  - Not affected by inoculum size
  - Acts on bacteria in stationary phase of growth
- IVIG (in toxic shock syndrome)
  - Role of IVIG controversial
    - 1 observational study improved 7 and 30 day survival
    - Cases more likely than controls to get surgery and clindamycin
    - 1 RCT (21 pts) - no mortality benefit

Summary: Management of necrotizing skin and soft tissue infections

- Early surgical consult/ intervention
- Empiric antimicrobial therapy
  - Piperacillin/tazobactam or carbapenem (group A strep, other gram pos, gram negs and anaerobes)
    - Plus
  - Clindamycin
    (group A strep – toxin inhibition)
    - Plus
  - Vancomycin
    (MRSA)
Case 5

53 yo M ER physician with 9 day h/o progressive cellulitis of L forearm. Initially noted a pustule ➔ self I&D, started keflex + clindamycin x 4 days. Progressive erythema and drainage. Started IV vanco + ceftriaxone, no improvement after 3 days.

Further history...

• History of chronic “benign” neutropenia
• 3 weeks ago, trip to Arizona where cleared brush in order to replace a water drip line and scraped his arm
• 2 weeks ago, worked in home (Merced) vegetable garden clearing eggplant and pepper brushes
• 7 days ago, cleaned his fish tank
• No animal or tick bites
• Only recent travel to Arizona

All of the following are possible causes of his infection EXCEPT:

A. Mycobacterium marinum
B. Coccidioides immitis
C. Nocardia brasiliensis
D. Brucella melitensis
E. Sporothrix schenckii

Gram stain from wound culture

Nocardia brasiliensis
Nocardia

- Soil inhabitant
- Worldwide distribution
- Incubation period: <1-6 weeks
- Often with mild systemic symptoms
- *Nocardia brasiliensis* > *asteroides* for cutaneous disease
- Diagnosis: biopsy and culture
  - Partially acid-fast, gram variable branching rods.
- Treatment: TMP-SMX x 4-6 months

26 yo M with 6 week history of R hand papule ➔ ulcer
Multiple visits to ED and urgent care
Receives several courses of abx, no improvement

*Leishmania panamensis*
Which of the following reflect true infectious cellulitis?

A

B

C
Which of the following reflect true infectious cellulitis?

“Masqueraders” of Infectious Cellulitis

- Stasis dermatitis
- Superficial thrombophlebitis and deep venous thrombosis
- Contact dermatitis
- Insect stings/tick bites
- Drug reactions
- Gouty arthritis
- Foreign body reaction (e.g. surgical mesh, orthopedic implants)
- Lymphedema
- Malignancy (e.g. T-cell lymphoma)
Summary

- Drainage/debridement is the mainstay of therapy of all purulent skin and soft tissue infections.
  - Uncomplicated abscess: Abx provide a modest benefit (~10%) over I&D alone
  - Uncomplicated outpatient:
    - Purulent SSTI – cover for MRSA (TMP-SMX or clinda)
    - Nonpurulent cellulitis: Cephalaxin, dicloxacillin, clindamycin
  - Complicated hospitalized – in most cases:
    - Cover for S. aureus and streptococci
    - Gram negative and anaerobic coverage unnecessary.
  - If no response to standard antibiotic therapy, consider alternative diagnoses (e.g. unusual infections, non-infectious etiologies). BIOPSY for culture and pathology.

Thank you!