Update in Management of Skin and Soft Tissue Infections

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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 cephalaxin

C. Incision and drainage plus TMP-SMX
IDSA Guideline Recommendations

• MRSA Guidelines (2011)
  - For a cutaneous abscess, I&D is the primary treatment. For simple abscesses or boils, 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 (AII)

• 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

Abscesses: Do antibiotics provide benefit over I&D alone?

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

Personal communication, Chip Chambers M.D.; Talan NEJM 2016

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

Personal communication, Chip Chambers M.D.; Talan NEJM 2016
Secondary Outcomes: NIH trials

- Chambers: Recurrence Rates after 1 month:
  - Clinda (7%) vs TMP/SMX (14%) vs placebo (12%)
  - Clindamycin resistance associated with Rx failure

- Talan: Complications

<table>
<thead>
<tr>
<th></th>
<th>TMP-SMX</th>
<th>Placebo</th>
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<tbody>
<tr>
<td>New infected site at TOC</td>
<td>3.1%</td>
<td>10.3%*</td>
</tr>
<tr>
<td>Surgical procedure at TOC</td>
<td>3.4%</td>
<td>8.6%*</td>
</tr>
<tr>
<td>Infection in household member</td>
<td>1.7%</td>
<td>4.1%*</td>
</tr>
<tr>
<td>Invasive infection</td>
<td>0.4%</td>
<td>0.4%</td>
</tr>
<tr>
<td>GI side effects</td>
<td>42.7%</td>
<td>36.1%</td>
</tr>
<tr>
<td>Rx d/c due to AE</td>
<td>1.9%</td>
<td>0.6%</td>
</tr>
</tbody>
</table>

*p<.05  Personal communication, Chip Chambers, M.D.; Talan NEJM 2016

Insert NEJM poll results (N=767)

- 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

Summary

- Cure rates among patients receiving I&D alone are high; antibiotics provide a modest benefit for treatment of uncomplicated abscesses
- Shared decision-making approach with patients?
  - Benefits: Slightly ↑ cure rates, ↘ repeat I&D, skin infxn at new site, infxn in household memers
  - Risks: adverse drug reaction, renal/ electrolyte problems, C. difficile
Empiric PO Antibiotics for Purulent SSTIs (MRSA active agents)

<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>$16</td>
</tr>
<tr>
<td>Daptomycin IV</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 q12h</td>
<td>7-14 days</td>
<td>$310</td>
</tr>
<tr>
<td>Ceftraroline 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 one wk later, over 30 min</td>
<td>8 days</td>
<td>$3000/ $1500</td>
</tr>
</tbody>
</table>

FDA Approved Agents for Treatment of Complicated SSTI

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


Slide courtesy of Chip Chambers, M.D.
Microbiology of SSTI: Hospitalized Patients

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>SA or strep</td>
<td>97%</td>
</tr>
<tr>
<td>SA or strep only</td>
<td>74%</td>
</tr>
<tr>
<td>S. aureus</td>
<td>5%</td>
</tr>
<tr>
<td>Streptococci</td>
<td>3%</td>
</tr>
<tr>
<td>Gram neg</td>
<td>2%</td>
</tr>
<tr>
<td>Anaerobes</td>
<td>1%</td>
</tr>
</tbody>
</table>

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

Antibiotic Utilization Among Hospitalized Patients with SSTI: Baseline

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vancomycin</td>
<td>40%</td>
</tr>
<tr>
<td>Gram negative</td>
<td>28%</td>
</tr>
<tr>
<td>Anti-pseudomonal</td>
<td>12%</td>
</tr>
<tr>
<td>Anti-anaerobic</td>
<td>12%</td>
</tr>
</tbody>
</table>

N=169

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

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Baseline</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vancomycin</td>
<td>p&lt;.001</td>
<td>p&lt;.01</td>
</tr>
<tr>
<td>Gram negative</td>
<td>p=.02</td>
<td>p&lt;.01</td>
</tr>
<tr>
<td>Anti-pseudomonal</td>
<td>p=.01</td>
<td></td>
</tr>
<tr>
<td>Anti-anaerobic</td>
<td>p=.01</td>
<td></td>
</tr>
</tbody>
</table>

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/periorbital infections, critically ill pts with necrotizing SSTI, animal bites, water exposure, severe diabetic foot
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?

β-hemolytic strep vs. S. aureus?

- Prospective study, hospitalized patients (N=248)

  Methods
  - Acute and convalescent titers (ASO and anti-DNaseB)
  - Rx with β-lactam antibiotics (cefazolin/oxacillin)

  Results
  - 73% due to β-hemolytic strep; 27% none identified
  - 96% response rate to β-lactam antibiotic

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


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

IDSA Guidelines on SSTI. 2014

Tedizolid
Dalbavancin
Oritavancin

S aureus (MRSA)

EMPIRIC RX

Tedizolid
Dalbavancin
Oritavancin

EMPIRIC Rx

- Vancomycin or
- linezolid or
- Televan or
- Clindamycin

EMPIRIC Rx

- TMP/SMX or
- Desoglymine

EMPIRIC Rx

- MSSA
- Vancomycin or
- Dalbavancin or
- Oritavancin

DEFINED Rx

- MSSA
- Linezolid or
- Televan or
- Clindamycin

I&D C&S

+ TMP/SMX or clinda
Cephalexin vs. Cephalexin + TMP-SMX in patients with Uncomplicated Cellulitis

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

Case 3

- Patient presents with 4th abscess in 4 months
- Prior abscesses 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. Give daily low dose clindamycin

How to Manage Recurrent Skin and Soft Tissue Infections?

Decolonization strategies

- 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

Fritz SA. Infect Control Hosp Epi. 2011
**Recurrent SSTI among Cases and Household Contacts**

*Mupirocin plus chlorhexidine*

<table>
<thead>
<tr>
<th>SSTI</th>
<th>1 mo</th>
<th>3 mo</th>
<th>6 mo</th>
<th>12 mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individual</td>
<td>0%</td>
<td>20%</td>
<td>40%</td>
<td>80%</td>
</tr>
<tr>
<td>Household</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

*Fritz CID 2012; 54: 743-51*

**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=.01
  - After treatment stopped, no difference

*Thomas NEJM 2013; 368: 1695-701*

**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)*

*Stevens CID 2014*

**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?**

![Cumulative Survival Rate Graph](image_url)

Mortality rate: > 30%

*Wong DH, Jour of Bone and Joint Surg, 2003*
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

Which of the following reflect true infectious cellulitis?

A

Which of the following reflect true infectious cellulitis?

B

Which of the following reflect true infectious cellulitis?

C
Which of the following reflect true infectious cellulitis?

Which of the following reflect true infectious cellulitis?

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: Cephalexin, clindamycin, TMP-SMX

• 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!