Skin and Soft Tissue Infections for the Internist

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No Disclosures
Skin and Soft Tissue Infections (SSTIs) Learning Objectives

• Review the optimal management of purulent and non-purulent cellulitis
• Understand the differential diagnosis of cellulitis
• Learn the clinical findings suggestive of necrotizing skin and soft tissue infections
• Understand when and how to evaluate diabetic foot ulcers for infection
Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by the Infectious Diseases Society of America

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Purulent Skin and Soft Tissue Infections
Cutaneous Abscesses

- Pus within deeper dermis and subcutaneous tissues
  - Surrounding cellulitis may be significant

- Microbiology
  - Monomicrobial *Staph aureus* including CA-MRSA
  - Polymicrobial (regional skin flora)

- Mainstay of therapy: incision and drainage (I&D)
  - Adequacy of drainage; loculation of adhesions
  - Cure rates with I&D alone high (70-85%)
  - Gram stain and culture recommended

- Imaging may be useful in certain circumstances

- Growing body of data supports adjunctive antimicrobial therapy

Evidence from Randomized Controlled Trials (RCTs)

- Two large RCTs, >2000 patients
- All patients underwent I&D (45-50% MRSA)
- Trimethoprim-sulfamethoxazole (TMP/SMX) vs placebo
  - Greater likelihood of abscess cure with TMP/SMX
  - Lower recurrence, need for hospitalization, need for surgery, spread within household with TMP/SMX
- TMP/SMX vs clindamycin vs placebo
  - Both clinda and TMP/SMX better than placebo for abscess cure
  - Fewer recurrences with clindamycin but less well tolerated

Daum et al. Abstract 1684. IDWeek 2016; New Orleans
Antibiotic Treatment for Purulent SSTIs

<table>
<thead>
<tr>
<th>Mild-moderate infection</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trimethoprim/sulfamethoxazole</td>
<td>1-2 DS BID</td>
</tr>
<tr>
<td>Doxycycline or Minocycline</td>
<td>100 mg PO BID</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>300 – 450 mg PO TID-QID</td>
</tr>
<tr>
<td>Severe infection</td>
<td>Dose</td>
</tr>
<tr>
<td>Linezolid</td>
<td>600 mg PO/IV BID</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>15-20 mg/kg IV q8-12°</td>
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</tbody>
</table>

- Culture is recommended to guide therapy
- Dosing and duration not well studied
CA-MRSA: Prevention of Recurrence

• 25-50% of patients with CA-MRSA have recurrences

• Traditionally recurrences attributed to autoinoculation
  – However nasal colonization not always present
  – Other sites (rectal, inguinal, axillary, oropharyngeal) may be more important

• Increasing emphasis on reacquisition as risk for recurrence
  – From household or other contacts
  – From fomites in the environment
CA-MRSA: Prevention of Recurrence

• Decolonization studies have been disappointing
  – Decolonization of entire household may be more effective than decolonizing the patient alone

• Consider decolonization if recurrence persists or evidence of transmission among household members
  – 2% nasal mupirocin twice daily 5-10 days
  – 4% topical chlorhexidine for 5-14 days or dilute bleach bath (¼ cup per ¼ tub) twice weekly for 3 months
  – Oral antibiotics generally not recommended

• Role of environmental decontamination unknown
  – Household colonization a predictor of recurrence

Liu et al. Clin Infect Dis 2011; 52: 1
Nonpurulent SSTIs

Cellulitis

Infection of the reticular dermis and subcutaneous fat

<table>
<thead>
<tr>
<th>ANATOMY</th>
<th>SYNDROME</th>
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<tbody>
<tr>
<td>Epidermis</td>
<td>Erysipelas</td>
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<tr>
<td></td>
<td>Impetigo</td>
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<tr>
<td></td>
<td>Folliculitis</td>
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<td></td>
<td>Ecthyma</td>
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<td></td>
<td>Furunculosis</td>
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<tr>
<td></td>
<td>Carbunculosis</td>
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<tr>
<td>Dermis</td>
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<tr>
<td></td>
<td>Cellulitis</td>
</tr>
<tr>
<td></td>
<td>Necrotizing fasciitis</td>
</tr>
<tr>
<td>Superficial fascia</td>
<td></td>
</tr>
<tr>
<td>Subcutaneous tissue</td>
<td></td>
</tr>
<tr>
<td>Subcutaneous fat, nerves, arteries, veins</td>
<td>Myonecrosis (clostridial and non-clostridial)</td>
</tr>
<tr>
<td>Deep fascia</td>
<td></td>
</tr>
<tr>
<td>Muscle</td>
<td></td>
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</tbody>
</table>
Empiric therapy of nonpurulent cellulitis

• Mild:
  – Typical cellulitis without systemic signs of infection
  – Initial oral therapy appropriate

• Moderate:
  – As in mild infection, but with systemic signs of infection
  – Initial IV therapy with transition to PO when systemic symptoms resolve and cellulitis recedes

• Severe:
  – Progressive skin changes, hemodynamic instability, organ system dysfunction, immunocompromise
  – Broad IV empiric therapy and consideration for surgery

Nonpurulent Cellulitis in the era of CA-MRSA

- Treatment of nonpurulent cellulitis is empiric
  - Blood cultures positive < 5%
  - Skin biopsy low yield
- Most noncultureable cellulitis is due to pyogenic streptococci (70-75%)
- β-lactam therapy remains optimal with high cure rates
  - Inpatient and outpatient clinical studies
- MRSA should be considered if:
  - Penetrating trauma, illicit drug use, prior MRSA, and in severe infection

Bruun et al. Open Forum Infect Dis 2016; 63:1034
## Mild-Moderate Nonpurulent Cellulitis: IDSA

<table>
<thead>
<tr>
<th>Oral Antibiotic</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin VK</td>
<td>250-500 mg PO QID</td>
</tr>
<tr>
<td>Cephalexin</td>
<td>500 mg PO QID</td>
</tr>
<tr>
<td>Dicloxacillin</td>
<td>500 mg PO QID</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>300-450 mg PO QID</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Intravenous Antibiotic</th>
<th>Dose</th>
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</thead>
<tbody>
<tr>
<td>Penicillin</td>
<td>2-4 million units IV q4-6°</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>1 gram IV q24°</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>1 gram IV q8°</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>600 mg IV q8°</td>
</tr>
</tbody>
</table>

Gram-Negative Cellulitis

- **Host Risk Factors:**
  - Diabetes, peripheral vascular disease, chronic liver disease, pre-existing ulceration, immunocompromise

- **Relevant Exposures:**
  - Saltwater or freshwater, animal bites

- **Organisms:**
  - *E. coli, Klebsiella, Campylobacter, Vibrio, Aeromonas, Pasteurella*

- **Empiric coverage for Gram-negative organisms recommended for:**
  - Severe cellulitis including septic physiology
  - Appropriate epidemiologic risk factors
Vibrio species

- Found in shellfish
- Seasonal (summer months)
- Comorbidities common (liver disease)
- Cutaneous injury with saltwater exposure
- Ingestion of raw oysters (septicemia)
- Clinically: hemorrhagic bullae, rapid necrosis and ulceration, gangrene
- Treatment: doxycycline + ceftriaxone
- Mortality high (17-53% for vulnificus species)

Haq. Am J Gastroenterol 2005;100:1195
Prevention of Cellulitis

• Risk of recurrence 16-30%
  – Cellulitis leads to impaired lymphatic function
  – Impaired lymphatic function predisposes to cellulitis

• Address Modifiable Risk Factors
  – Treat stasis / lymphedema
  – Treat underlying skin disease
    • intertrigo
  – Optimize diabetes control
  – Assess vasculature
  – Wound care

Oh et al. J Infect 2014;69:26
Prevention of Cellulitis: 
Antibiotic Prophylaxis

• Antibiotic prophylaxis reduces the risk of recurrent cellulitis
  – Risk ratio 0.46
  – Daily oral or monthly IM penicillin
    • Alternative: erythromycin
  – Benefit only accrues while on antibiotics

• Unanswered Questions
  – When to start prophylaxis
  – Optimal antibiotic dosing and duration
  – Strategies if penicillin prophylaxis fails and in penicillin allergy

• IDSA: consider 3-4 annual episodes

Oh et al. J Infect 2014;69:26
Diabetic Foot Infections
Infection in Diabetic Foot Ulcer

- Not all diabetic ulcerations are infected
- Infection remains a clinical diagnosis
  - Purulence, erythema, warmth, tenderness, induration
- Fever and leukocytosis are often absent
- Neuropathy and ischemia can both mask and mimic infection
- All ulcers are colonized with bacteria
  - Presence of bacteria does not imply infection
  - No evidence that antimicrobial treatment of noninfected ulcers facilitates wound healing or prevents infection
Management of Diabetic Foot Infections (DFI)

• Assess the severity of infection
• Determine the bacterial etiology
  – Culture-derived therapy leads to improved outcomes
• Assess the need for surgical debridement
• Consider additional investigation for osteomyelitis
• Initiate antibiotic therapy
• Attend to risk factors
DFI: Severity of Infection

- **Mild**
  - cellulitis/erythema extends ≤ 2 cm around the ulcer
  - Limited to skin and superficial soft tissues

- **Moderate**
  - Cellulitis > 2 cm around the ulcer
  - Lymphangitic streaking
  - Extension below superficial fascia (muscle, tendon, joint, bone)

- **Severe**
  - With systemic toxicity or metabolic instability

Diagnosis of Osteomyelitis

• 50-60% of serious diabetic foot infections are complicated by osteomyelitis

• Presence of osteomyelitis can inform:
  – need for surgical debridement
  – route and duration of antibiotic therapy
  – Increased risk of limb amputation

• Consider evaluation for osteomyelitis if:
  – Severe infection
  – Longstanding (>30 days) or large (>2 cm) wounds
  – Recurrent infection around ulcer

Osteomyelitis Diagnosis: Pearls

• Gold standard: Bone culture > histopathology
• Probe to bone test (if done properly) can rule in osteomyelitis in high risk patients, rule out in low risk
  – sensitivity 0.87; specificity 0.83; PPV 0.91; NPV 0.84
• ESR >70 is useful but insufficiently sensitive
• Serial radiography has not been well studied but is likely to be useful in chronic wounds and milder infections
• Bone scan has poor specificity (0.28)
• MRI is the most accurate radiographic test in the evaluation of osteomyelitis (sensitivity 0.90; specificity 0.79)

Weiner J Foot Ankle Surg 2011;50:197
Lam Clin Infect Dis 2016;63:944
DFI: Antibiotic Therapy

• Culture-directed antibiotic therapy leads to improved outcomes
  – Culture by biopsy or curettage after debridement
  – Reduced likelihood of later amputation
• Empiric coverage for sensitive *Staph aureus* and pyogenic streptococci in all diabetic foot infections
• Consider risk factors for MRSA
  – prior antibiotic exposure, previous hospitalization, wound duration, prior MRSA infections, local MRSA prevalence
• Consider risk factors for *Pseudomonas aeruginosa*
  – warm climates, water exposure

Senneville. Diabetes Care 2008;31:637
DFI: Role of Surgery

• Role and type of surgery not systematically defined
  – Principle: Antibiotics and host immune cells do not reach devascularized tissues
  – Surgery increases likelihood of cure but may lead to important biomechanical changes
  – Retrospective data demonstrates many patients can be cured without surgery (antibiotics for 12 weeks)
  – Those who fail antibiotic therapy may require higher level amputation

• Surgery generally accepted for:
  – Abscess, extensive bone or synovial involvement, gangrene, necrotizing soft tissue infection
Necrotizing Fasciitis

- Necrosis of deep and/or superficial fascia, along with deeper dermis, subcutaneous tissues and muscle
  - Microvascular thrombosis leads to ischemia
- Characterized by clinical urgency and high mortality
  - A “can’t miss” diagnosis
Necrotizing Fasciitis

- **Necrotizing Fasciitis Type 1 (2/3 of cases)**
  - Polymicrobial: gram positives, gram negatives, anaerobes
  - Host risk factors common: diabetes, peripheral vascular disease, illicit drug use
  - Setting: Trauma, abdominal injury, surgery;
  - Perineal infection (Fournier’s)

- **Necrotizing Fasciitis Type 2 (1/3 of cases)**
  - Monomicrobial: GAS > Groups B, C, G streptococcus > *Staph aureus*; consider also Vibrio and Aeromonas species
  - Often a normal host
  - Minor trauma may predispose
  - Limbs predominate
Necrotizing Fasciitis: Clinical Clues

- Woody induration and pain of subcutaneous tissue beyond area of skin involvement
- Pain and toxicity out of proportion to local findings
- Rapid extension of skin changes: progressive discoloration, ecchymoses and bullae, frank gangrene
- Rapid progression despite antimicrobial therapy
- Anesthesia
- Systemic toxicity
- Multiple laboratory derangements: rise in CPK, creatinine, leukocytosis, thrombocytopenia, acidosis
- Diagnosis confirmed only by surgical exploration
Necrotizing Fasciitis

Case Records of the Massachusetts General Hospital. NEJM 2009;360:281
Necrotizing Fasciitis: Management

• Surgical Debridement
  – Source control
  – Early surgery increases survival (by up to ninefold)
  – Early surgical reassessment at 24-36 hours and as needed thereafter

• Antimicrobial Therapy
  – Polymicrobial: broad spectrum against gram-positives, gram-negatives, anaerobes; clindamycin preferred
  – Group A Streptococcus (*pyogenes*): Penicillin plus Clindamycin
  – Duration of therapy: 10-14 days

• Intravenous immunoglobulin if associated with toxic shock syndrome (GAS)

Clostridial Myonecrosis (Gas Gangrene)

- Necrotizing Myositis
- Clostridium inoculated into anaerobic environment
  - Traumatic (*Clostridium perfringens*)
  - Bacteremic (*Clostridium septicum*)
    - Usually occult GI malignancy
    - Toxin production leads to cascade of ischemia and necrosis
- Clinical: rapidly progressive pain and swelling
  - Bullae may develop, +/- crepitus; sepsis
- High mortality (up to 80%)
- Rx: penicillin/clindamycin; amputation / disarticulation
Cellulitis that doesn’t improve…

- 50 year old man with a neuropathic diabetic foot ulcer
  - 5 days of right foot swelling and fever
Common causes of Pseudocellulitis:

- 28-33% of patients admitted with cellulitis misdiagnosed
- Pseudocellulitis causes:
  - Stasis dermatitis (most common misdiagnosis)
  - Inflammatory (panniculitis, connective tissue disorders)
  - Malignancy (carcinoma erysipeloïdes, leukemia cutis, Paget’s of breast)
  - Neutrophilic dermatoses (e.g. Sweet syndrome)
  - Contact dermatitis
  - Radiation dermatitis
  - Metabolic (e.g. gout)
  - Drug reactions
  - Insect bites

Raff and Kroshinsky. JAMA 2016;316:325
Which of these is cellulitis?

- Erythema migrans
- Cellulitis
- Hematoma
- Calciphylaxis
- Stasis Dermatitis
- Deep vein thrombosis

Raff and Kroshinsky. JAMA 2016; 316:325
Clues to Pseudocellulitis

- Gradual onset of symptoms
- Pruritus
- Bilateral lower extremity involvement
- Lack of temperature change between extremities
- Frequent recurrences after discharge
- Failure to resolve with beta-lactam therapy
- Measures of inflammation not useful
  - Leukocytosis, fever, and inflammatory markers
- “Diagnostic” trial off antibiotics
Take Home Points

- Management of soft tissue infections hinges on presence of purulence and clinical assessment of severity.
- For non-purulent cellulitis, beta-lactam therapy is optimal.
- For purulent cellulitis, antibiotics are now recommended for abscess treatment including empiric MRSA coverage.
- Culture to guide therapy whenever possible.
  - CA-MRSA, diabetic foot infections.
- Consider and recognize signs of necrotizing soft tissue infection.
- Consider non-infectious explanations when cellulitis does recur or does not resolve.