Osteomyelitis & Diabetic Foot Ulcer

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Objectives

- To describe the pathogenesis and clinical characteristics of osteomyelitis
- To identify the most likely etiologic agent for osteomyelitis
- To suggest appropriate empiric and definitive antimicrobial therapy for osteomyelitis
- To describe pathogenesis and clinical characteristics of diabetic foot ulcers
- To identify the most likely etiologic agent for diabetic foot ulcers
- To suggest appropriate empiric and definitive antimicrobial therapy for diabetic foot ulcers
Osteomyelitis

- Inflammation of bone marrow and surrounding bone
- Almost always due to infecting organism
- Infection by three routes:
  - Hematogenous spread
  - Direct infection from contiguous source
  - Infection of bone due to vascular insufficiency (diabetic foot ulcer could lead to this)
Osteomyelitis

- Capillaries in epiphyseal growth plate near the end of bone have sharp loops
  - Capillaries enter into larger veins, where blood flow slows, can allow bacteria to settle
- Edema and inflammation associated with infectious process can compromise blood flow, lead to necrosis
- Necrosis can lead to sequestra (devitalized bone that has separated from healthy bone)
Osteomyelitis

- Surgery often important part of treatment, esp. if devitalized bone present, abscess, etc.
- Important to get specific microbiologic diagnosis
Hematogenous Osteomyelitis

- Result of seeding from blood
- More common in infants & children (< 16 years)
- Frequently involve metaphyses of long bones
- Bacteria
  - most common organism: S. aureus (60-90%)
  - GNB (E. coli, Klebsiella, Proteus, Pseudomonas)
  - group B streptococci
  - Salmonella
Hematogenous Osteomyelitis

- Abrupt onset of high fever, malaise, localized pain, tenderness, swelling, decreased motion
- X-ray changes lag clinical features by 2 wks
  » Bone scan may be helpful
- Lab abnormalities: Increased ESR, WBC
- Risk factors: anything promoting bacteremia (indwelling catheter, IVDA)
Hematogenous Osteomyelitis

- Blood and bone aspirate culture before antibiotics, change empiric therapy on results
- Antibiotics (start ASAP, IV, high doses)
  - Newborn (< 4 mo)
    - *S. aureus*, GNB, group B strep
    - Nafcillin (150 mg/kg/day [QID]) + cefotaxime (50 mg/kg q 6 hr)
  - Child
    - *S. aureus*, group A strep, rarely coliforms
    - Nafcillin + cefotaxime (if GNB on gram stain)
  - Adult (>21 years)
    - *S. aureus*
    - Nafcillin, cefazolin
Hematogenous Osteomyelitis

- **Duration of antibiotics**
  - 4-6 weeks

- **Oral antibiotics**
  - Always start with IV (usually continue about 2 wks)
  - In kids, can switch to PO when there is clinical improvement, decrease in signs of inflammation, and patient afebrile 3 days
  - Candidates should have:
    - Disease of recent onset
    - Identification of infecting organism
    - Enforced compliance
    - Surgery as needed
Contiguous Osteomyelitis

- Direct infection of bone from exogenous source or spread from adjacent tissue
- Common etiology: history of surgery for an open reduction of a fracture
- Usually in adults over 50 (due to factors such as more hip fracture, ortho procedures, etc.)
- Bacteria
  - *S. aureus*
  - *Pseudomonas* (e.g., puncture to foot)
  - *Proteus*
  - *Klebsiella*
  - *E. coli*
  - anaerobes (may be in mixed infection; *Bacteroides*)
Contiguous Osteomyelitis

- Systemic signs not usually present (unlike hematogenous)
  - Most frequent symptom: pain in area of infection
- Local tenderness, swelling, erythema, decreased motion
- Treatment should be based on culture of bone biopsy
Contiguous Osteomyelitis

- Empiric therapy (while awaiting results)
  - Post reduction & internal reduction of fracture
    - *S. aureus*, coliforms, *P. aeruginosa*
      - Nafcillin 2 g q 4 hr IV + ciprofloxacin 750 mg BID PO
      - Nafcillin 2 g q 4 hr IV + ceftazidime 2 g IV q 8 hr
  - Post-op infection of prosthetic joint
    - *S. epidermidis, S. aureus*, Enterobacteriaeaeceae
      - Vancomycin + ciprofloxacin

- 4-6 weeks of antibiotic therapy

- Vascular insufficiency
  - Difficult to manage: freq. req. amputation
  - Broad spectrum antibiotics
    - Nafcillin + ceftazidime
    - Also consider anaerobic coverage
Chronic Osteomyelitis

- Inadequate treatment of acute osteomyelitis can lead to sequestra, recurrent symptoms
- Therapy based on results from bone biopsy
- Surgery has important role in removing all sequestra, necrotic areas
- Parenteral therapy 4-6 weeks, follow with 1-2 months oral antibiotics
Osteomyelitis: Special Cases

- **IVDA**
  - 50% of osteomyelitis cases are vertebral
  - Usually gram-negative: *P. aeruginosa, Klebsiella, Enterobacter, Serratia.*
  - Nafcillin + ciprofloxacin

- **Sickle cell anemia patients**
  - *Salmonella*
  - Usually in long bones
  - Ciprofloxacin
Vertebral Osteomyelitis

- Pts in 50-60s
- Lumbar, thoracic regions
- 60% due to staph
- *E. coli* also important cause; from urinary tract
- Cefazolin
Prophylaxis in Bone Surgery

- Administer antibiotics IV 30 minutes prior to incision of the skin and for no longer than 24 hours after the operation.
- In orthopedic surgery for closed fractures, antistaphylococcal penicillins and first- or second-generation cephalosporins are indicated.
- In patients who can receive antibiotics within 6 hours after trauma and who receive prompt operative treatment, a first or second generation cephalosporin for one day is appropriate.
- Complex fractures with extensive soft tissue damage requires broader antimicrobial coverage for longer duration.
59 year old male suffered severe leg fracture two weeks ago.

Fracture set by open reduction, completed a 7 day course of cefazolin, started on day of surgery

2 days ago, developed pain, swelling in calf
  » Calf tender, warm, swollen, erythematous
  » Patient afebrile

All laboratory findings WNL

Bone scan consistent with left tibial inflammation, due to healing or infection
Osteomyelitis Case

- What findings are consistent with osteomyelitis?
  - History of surgical repair of fracture
  - Local pain, tenderness, erythema
  - Absence of systemic signs, labs WNL?
- Should he have cultures done?
  - Yes—requires surgical exploration, and biopsy of bone at infected site, and blood cultures
- What antibiotics while waiting for culture result?
  - S. aureus most common, must consider enteric GNB (esp. since pt. had cefazolin previously)
  - Nafcillin + ceftazidime
Diabetic Foot Ulcer

- Foot infections among most common and severe complications of DM; LE ulcer most frequent reason for hospitalization in DM\(^{(1, 1A)}\)

- DM leading cause of lower-extremity amputations in U.S.\(^{(2-3)}\)

- Retrospective studies indicate a 2-year mortality rate of 35-50% and a cumulative amputation rate over 1-3 years of 40%\(^{(4)}\)
  
  » Almost all subsequent amputations precipitated by previous foot ulcer-stressing need for preventative foot care

- At 2 years, relative risk of death 2.4x in diabetic subjects with foot ulcers compared to those without\(^{(5)}\)

\(^{(1)}\) CID 1997;25:1318-26 \(^{(1A)}\) J Amer Geriatrics Soc 48 (7)  
\(^{(2)}\) MMWR 1991;40:737-739 \(^{(3)}\) MMWR 1993;42:1-20  
Pathogenesis

- **Neuropathy**
  - Sensory—aren’t aware of mechanical/thermal injury
  - Motor—predisposition to gait disturbance/foot deformities, leading to weight maldistribution, elevated focal pressure, risk of ulceration
  - Autonomic—interferes with sweating, causes dry, cracked skin

- **Vascular insufficiency**—diminished arterial blood supply

- **Poorly characterized defects in host immunity**
Risk Factors for Ulcers/Amputations

- DM > 10 years
- Male
- Poor glucose control
- CV, retinal or renal complications
- Peripheral neuropathy
- Altered biomechanics
  - Evidence of increased pressure (callus, erythema, hemorrhage under callus)
- Peripheral vascular disease
- History of ulcer or amputation
Diabetic Foot Ulcers
<table>
<thead>
<tr>
<th>Severity</th>
<th>Characteristics</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild (non-limb threatening)</td>
<td>• Superficial ulceration</td>
<td>• Oral Antibiotics</td>
</tr>
<tr>
<td></td>
<td>• Purulent drainage</td>
<td>• Local podiatry care</td>
</tr>
<tr>
<td></td>
<td>• Minimal/absent cellulitis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• No osteomyelitis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• No systemic toxicity</td>
<td></td>
</tr>
<tr>
<td>Moderate to severe (limb-threatening)</td>
<td>• Ulceration to deep tissues</td>
<td>• IV antibiotics</td>
</tr>
<tr>
<td></td>
<td>• Purulent discharge, Cellulitis</td>
<td>• Surgical drainage</td>
</tr>
<tr>
<td></td>
<td>• Systemic toxicity</td>
<td>• Prolonged antibiotic therapy and/or bone resection</td>
</tr>
<tr>
<td></td>
<td>• Mild/moderate necrosis</td>
<td>• Assess need for revascularization</td>
</tr>
<tr>
<td></td>
<td>• Presence/absence of osteo</td>
<td></td>
</tr>
<tr>
<td>Severe (life-threatening)</td>
<td>• Ulceration to deep tissues</td>
<td>• Urgent Surgical need</td>
</tr>
<tr>
<td></td>
<td>• Purulent drainage, Cellulitis</td>
<td>• Amputation potential</td>
</tr>
<tr>
<td></td>
<td>• Systemic toxicity (shock)</td>
<td>• IV broad-spectrum abx</td>
</tr>
<tr>
<td></td>
<td>• Marked necrosis/gangrene</td>
<td>• Control hyperglycemia</td>
</tr>
<tr>
<td></td>
<td>• Osteomyelitis?</td>
<td>• Control ketoacidosis</td>
</tr>
<tr>
<td></td>
<td>• Bacteremia?</td>
<td>• Assess need for revascularization</td>
</tr>
</tbody>
</table>
Microbiology

- Polymicrobial
  - Aerobic and anaerobic gram-negative bacilli
  - Gram-positive and gram-negative cocci
  - Between 45% and 85% are polymicrobial
  - Usually 3-5 organisms isolated per infection in hospitalized patients

- *Staphylococci* most common, followed by *Streptococci*

- Gram-negative bacilli and/or anaerobes occur in approximately 50% of cases
## Microbiology

### Aerobic gram-positive cocci
- *S. aureus*
- *S. epidermidis*
- *Enterococcus* spp.
- *Streptococcus* spp.
- *Corynebacterium* spp.

### Aerobic gram-negative bacilli
- *Proteus*
- *Enterobacter*
- *E. coli*
- *Klebsiella*
- *Pseudomonas* spp.

### Obligate Anaerobes
- *Peptococci/Peptostreptococci*
- *Bacteroides*
- *Clostridium*
- Other species
Antibiotic Therapy

- **Empiric-oral (mild-moderate infection)**
  - Amox/clavulanic acid
  - TMP/SMX
  - Clindamycin
  - Clindamycin + ciprofloxacin
  - Dicloxacillin
  - Cephalexin
  - Ciprofloxacin
  - No improvement at 48-72 hrs, start IV

- **Empiric-IV (mod-severe Infection)**
  - Ampicillin/sulbactam
  - Pipercillin/tazobactam
  - Ampicillin + clindamycin
  - Metronidazole + AG
  - Imipenem/cilastatin
  - Cefoxitin or cefotetan
  - Ciprofloxacin
  - 3rd generation cephalosporin
Antibiotic Therapy

- IV antibiotics for life-threatening infections (include *P. aeruginosa* coverage)
  - Ampicillin/sulbactam + aminoglycoside
  - Piperacillin/tazobactam + aminoglycoside
  - Ampicillin + clindamycin + aminoglycoside
  - Imipenem/cilastatin + aminoglycoside
Enterococcus spp.

- Not a common pathogen
  - Empiric therapy only required for severe, necrotizing infection
  - Unless it is the predominant organism, may not need enterococcal coverage

- NO enterococcal coverage
  - Clindamycin
  - Cephalosporins
  - Ticarcillin

- Consider
  - Penicillin
  - Ampicillin
  - Pipercillin
  - Imipenem/cilastatin
  - Vancomycin
Other Microorganisms

- *Pseudomonas aeruginosa*
  - Pipercillin
  - Ceftazidime
  - Imipenem/cilastatin
  - Ciprofloxacin
  - Trovafloxacin
  - Tobramycin

- MRSA
  - Vancomycin
  - Linezolid/Synercid
Factors Affecting Antibiotic Selection & Efficacy

- Vascular impairment - penetration of antibiotics
- Impaired renal function - caution with aminoglycosides
- Autonomic neuropathy & gastroparesis - decreased absorption of oral antibiotics
- Local antimicrobial resistance patterns
- Drug allergies - penicillin allergies
Duration of Therapy

- Depends upon
  - Infection severity
  - Causative organism
  - Clinical response

- 2-3 weeks for soft tissue infections
- 4-6 weeks if osteomyelitis

- Infections often recur; can be years after apparently successful therapy
Prevention

- All with DM should get exam at least yearly, including:
  - Assessment of protective sensation
  - Assessment of foot structure/biomechanics
  - Assessment of vascular status, skin integrity
- All with neuropathy should get visual inspection of feet at every visit with health care professional
- Correct fitting footwear
- Patients should monitor feet daily

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Diabetic Foot Ulcer Case

- 67 year old male diabetic presents to general practitioner for routine checkup
- 15 year history of poorly controlled diabetes, 3 year history of recurrent foot ulcers
- Today, a previously healed ulcer is open, inflamed, and purulent fluid can be expressed from the wound
- Patient reports no pain, temperature normal, and no signs of systemic infection
Diabetic Foot Ulcer Case

- **Does he have an infection? Antibiotics required?**
  - Only infected wounds should be treated with antibiotics
  - Inflamed area with discharge indicates infection. Should be given antibiotics

- **Any other lab tests?**
  - Culture wound? Deep culture, aerobic/anaerobic
  - Tests to rule-out osteomyelitis

- **Surgery, debridement to remove necrotic and infected tissue considered by some to be the mainstay of treatment**
Diabetic Foot Ulcer Case

- **Antibiotic therapy**
  - Agent for moderate-severe infection—IV
    - Cefoxitin, cefotetan, ampicillin/sulbactam
  - Duration of therapy
    - At least 3-4 days after signs of infection are gone