Arthritis, Osteomyelitis, and Prosthetic Joint Infections

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DISCLOSURES
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  • None
  • Resolution

CASE #1

• This presentation was originally presented at the 2012 course.
• Minor edits have been made to this version of the presentation.
• The version in the audio recordings section was not edited.

CASE #1

□ 21-year-old female injection drug user and no significant PMH presents with fever and right-sided chest pain.
□ On exam, she is febrile to 102°F. She has a 2/6 systolic murmur that increases on inspiration, and swelling and tenderness over right sternoclavicular joint. Rest of examination is the normal.
□ Aspiration of the sternoclavicular joint reveals a small amount of purulent material. TEE shows a vegetation on the tricuspid valve.

EPIDEMIOLOGY OF BACTERIAL ARTHRITIS

□ 2-10 cases/100,000/year
□ 28-38 cases/100,000/year in those with rheumatoid arthritis
□ Published mortality 7-15%
□ Morbidity up to 50%
□ Usually hematogenously acquired; other routes are direct inoculation or contiguous spread

Pending culture results from blood and joint fluid, which of the following empiric antimicrobial regimens should be initiated?

A. Daptomycin + caspofungin
B. Nafcillin + gentamicin
C. Clindamycin + trimethoprim-sulfamethoxazole
D. Vancomycin + cefepime
E. Cefepime + gentamicin
**MICROBIOLOGY OF NONGONOCOCCAL SEPTIC ARTHRITIS**

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. aureus</td>
<td>37-65</td>
</tr>
<tr>
<td>Coag-negative staph</td>
<td>4</td>
</tr>
<tr>
<td>Streptoccci</td>
<td>22</td>
</tr>
<tr>
<td>Gram-negatives</td>
<td>5-20</td>
</tr>
<tr>
<td>Culture-negative</td>
<td>10-20</td>
</tr>
<tr>
<td>Polymicrobial</td>
<td>≤ 8</td>
</tr>
</tbody>
</table>

**CASE #2**

- 45-year-old man vacationing in Spain presents with fever, malaise, anorexia and left lower back pain; about 3 weeks earlier, he ingested unpasteurized milk while visiting a local farm.
- On exam, temperature is 101°F. He has tenderness over the left sacroiliac joint; the pain is accentuated with flexion and external rotation of the hip.
- Radiographs reveal blurring of the articular margins of the left sacroiliac joint and widening of the sacroiliac space.

**CASE #2**

Which of the following is the most likely etiology of this patient’s sacroiliitis?

A. Brucella melitensis
B. Mycobacterium bovis
C. Bacillus arthracis
D. Coxiella burnetii
E. Ankylosing spondylitis

**EPIEDEMOLOGY/Etiology of Nongonococcal Arthritis**

<table>
<thead>
<tr>
<th>Feature</th>
<th>Etiologic Agent(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatoid arthritis</td>
<td>S. aureus (~75%)</td>
</tr>
<tr>
<td>Injection drug use</td>
<td>S. aureus, P. aeruginosa</td>
</tr>
<tr>
<td>Diabetes, malignancy</td>
<td>S. aureus, group B streptococci</td>
</tr>
<tr>
<td>Immuno-compromised</td>
<td>S. aureus, strep, gram-negatives, Listeria monocytogenes</td>
</tr>
<tr>
<td>Fibrocartilagenous joints</td>
<td>S. aureus, P. aeruginosa</td>
</tr>
</tbody>
</table>

**EPIEDEMOLOGY/Etiology of Nongonococcal Arthritis**

<table>
<thead>
<tr>
<th>Feature</th>
<th>Etiologic Agent(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cat/dog bite</td>
<td>Pasteurella multocida, anaerobes</td>
</tr>
<tr>
<td></td>
<td>Capnocytophaga sp.</td>
</tr>
<tr>
<td>Human bite</td>
<td>Eikenella, anaerobes, oral flora</td>
</tr>
<tr>
<td>Rat bite</td>
<td>Streptobacillus moniliformis</td>
</tr>
<tr>
<td>Ingestions (goat cheese, unpasteurized milk, occupation)</td>
<td>Brucella sp.</td>
</tr>
<tr>
<td>Living/travel SE Asia</td>
<td>Burkholderia pseudomallei, Streptococcus suis</td>
</tr>
</tbody>
</table>

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CLINICAL FEATURES OF NONGONOCOCCAL ARTHRITIS
- Monoarticular in 80-90%; knee in 50%
- Pain and loss of function (>90%); swelling, redness, increased warmth
- Fever in 60-80%
- Focal joint tenderness, inflammation, effusion, limited and painful motion
- Symptoms and signs more subtle in the immunocompromised or those with RA

DIAGNOSIS OF NONGONOCOCCAL ARTHRITIS
- Arthrocentesis reveals purulent (>50,000 WBC/mm³), low viscosity fluid with increased neutrophils (>75%)
- Gram stain positive in up to 50%; depends on microorganism
- Synovial fluid cultures positive in 80-90%
- Blood cultures positive in 50-70%

EPIDEMIOLOGY OF DISSEMINATED GONOCOCCAL INFECTION (DGI)
- Sexually active adolescents and adults (<30 years of age)
- DGI produces two syndromes (may overlap)
  - Gonococcal arthritis
  - Tenosynovitis, dermatitis, polyarthralgia without purulent joint infection
- Less than half of the patients have a true septic arthritis
- 4 times more common in women
- Complicates 0.5-3% of cases of mucosal GC infection

PATHOGENESIS OF DGI
- Occult bacteremia secondary to mucosal infection of urethra, cervix, rectum, oropharynx
- DGI most likely results from asymptomatic mucosal infection; risk increases during menstruation, pregnancy, postpartum period
- Host factors – terminal complement deficiencies (C5-C8), systemic lupus erythematosus

CLINICAL FEATURES OF DGI
- Dermatitis (2/3 of patients)
  - Painless, nonpruritic, few in number
  - Macules, papules, and pustules on an erythematous base
- Tenosynovitis (2/3 of patients)
  - Usually in fingers, hands, wrists
  - Occurs simultaneously with rash
- Migratory polyarthralgia or polyarthritis
  - Asymmetric, severe joint symptoms

DIAGNOSIS OF DGI AND GONOCOCCAL ARTHRITIS
- Gonococcal arthritis
  - Synovial fluid WBC 50-100,000/mm³ (neutrophils)
  - Synovial fluid Gram stain positive in 25%
  - Synovial fluid culture positive in 50%
- DGI without suppurative arthritis
  - Synovial fluid WBC count lower
  - Synovial fluid cultures positive in 20-30%
  - Synovial fluid PCR sensitivity of 80%
**DIAGNOSIS OF DGI AND GONOCOCCAL ARTHRITIS**

- Positive blood cultures in <30%
- Culture yield of mucosal sites
  - Cervical swabs positive in 80-90% of women
  - Urethral swabs positive in 50-70% of men
  - Lower yields from rectal and oropharyngeal swabs, but may be positive

**EMPIRIC ANTIMICROBIAL THERAPY OF BACTERIAL ARTHRITIS**

<table>
<thead>
<tr>
<th>Risk Factor / Gram Stain</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Joint disease / GPC</td>
<td>Vancomycin (pending in vitro susceptibility)</td>
</tr>
<tr>
<td>Young &amp; sexually active / GNC</td>
<td>Ceftriaxone</td>
</tr>
<tr>
<td>GNR</td>
<td>Ceftazidime, cefepime, pip/tazo, carbapenem</td>
</tr>
<tr>
<td>Negative Gram stain</td>
<td>Vancomycin + either ceftazidime, cefepime, or a fluoroquinolone</td>
</tr>
</tbody>
</table>

**JOINT DRAINAGE FOR BACTERIAL ARTHRITIS**

- Gonococcal arthritis – not required
- Repeated needle aspiration
  - First 5-7 days until purulence is minimal
- Arthroscopy
  - Irrigation, lysis of adhesions, removal of purulent material
  - Effective for knee, shoulder, ankle
- Open surgical drainage
  - Hip joints
  - Poor response to therapy
  - Aspiration or arthroscopy impractical

**DURATION OF ANTIMICROBIAL THERAPY FOR BACTERIAL ARTHRITIS**

- IV therapy for 2-4 weeks
- 7-10 days for gonococcal arthritis
- 4 weeks generally for *S. aureus* (including MRSA) and gram-negative bacilli
- If gram-negative organism is sensitive to fluoroquinolones, oral therapy used in latter half of treatment course

**CASE #3**

- 30-year-old woman presents with acute onset of bilateral hand pain
- Married and monogamous; 4-year-old son with recent fever and rash; 2 cats, dog, parrot, snake, and rabbit; traveled to India 2 years ago
- Febrile to 39°C, bilateral pain and swelling in PIP and MCP joints
- WBC count is 3,500/mm³

Which of the following is the most likely etiology of the patient's illness?

A. Bartonella henselae  
B. Parvovirus B19  
C. Chikungunya virus  
D. Salmonella enteritis  
E. Pasteurella multocida

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### Viral Arthritis

<table>
<thead>
<tr>
<th>Agent</th>
<th>Percent of Cases</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rubella</td>
<td>51-61%</td>
<td>• No prior vaccination</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Symmetric polyarthritis</td>
</tr>
<tr>
<td>Parvovirus B19</td>
<td>60% of adult cases</td>
<td>• Unusual in children</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Sudden, severe polyarthritis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Small joints</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• May mimic RA</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>10-14%</td>
<td>• Associated rash</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>10-25%</td>
<td>• Severe, sudden onset symmetric polyarthritis in hands and knees</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>9-19%</td>
<td>• Controversial whether associated with inflammatory arthritis</td>
</tr>
</tbody>
</table>

### Reactive Arthritis

- Onset of inflammatory arthritis after an infection elsewhere in the body
- Enthesitis (Achilles tendonitis/plantar fasciitis)
- Microorganisms not cultured from synovial fluid
- Begins several weeks after antecedent infection
- Asymmetric oligoarticular arthritis
- Treatment is anti-inflammatory agents; role of antimicrobial therapy is controversial

### Reactive Arthritis with Extra-Articular Features

- Urethritis
- Conjunctivitis (bilateral and painful)
- Uveitis (unilateral and painless)
- Keratoderma blennorrhagium
- Circinate balanitis/vulvitis
- Lingual or oral ulcerations (painless)
- Nail dystrophy

### Case #4

- 80-year-old male with diabetes underwent right TKA 3 months ago for severe osteoarthritis presents with constant pain and swelling of his right knee.
- On exam, he is afebrile with normal vital signs. His right knee is painful, swollen, and there is decreased range of motion.
CASE #4

Which of the following is the best test for establishing that this patient has a prosthetic joint infection?

A. Radiograph of right knee  
B. Technitium bone scan  
C. Indium-labeled leukocyte scan  
D. Fluorodeoxyglucose PET Scan  
E. Aspiration and culture of joint fluid

EPIDEMIOLOGY OF PROSTHETIC JOINT INFECTIONS

- 1-3% of indwelling prostheses become infected
- Predisposing factors include prior surgery at prosthesis site, RA, immunocompromised state, diabetes, poor nutritional state, obesity, psoriasis, extremely advanced age
- Infection may be locally introduced or hematogenous (20-40% of cases)
- Any factor that delays wound healing increases risk of infection

ETIOLOGY OF PROSTHETIC JOINT INFECTIONS

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coag-negative staph</td>
<td>22-43</td>
</tr>
<tr>
<td>S. aureus</td>
<td>12-23</td>
</tr>
<tr>
<td>Streptococci</td>
<td>9-10</td>
</tr>
<tr>
<td>Enterococci</td>
<td>3-7</td>
</tr>
<tr>
<td>Gram-negative bacilli</td>
<td>5-25</td>
</tr>
<tr>
<td>Anaerobes</td>
<td>2-10</td>
</tr>
<tr>
<td>Mixed flora</td>
<td>10-20</td>
</tr>
<tr>
<td>Culture-negative</td>
<td>7-11</td>
</tr>
</tbody>
</table>

CLINICAL FEATURES OF PROSTHETIC JOINT INFECTIONS

- Early
  - Less than 3 months after surgery
  - Virulent organisms (S. aureus, gram-negative bacilli)
  - Coagulase-negative staphylococci, streptococci
- Delayed
  - 3-12 months after surgery
  - Caused by less virulent organisms (coagulase-negative staph, P. acnes), but may also be S. aureus
- Late
  - More than 12 months, including hematogenous seeding
  - Staphylococci (S. aureus and coag-negative), other skin commensals, gram-negative bacilli, anaerobes

CLINICAL FEATURES OF PROSTHETIC JOINT INFECTIONS

- Most patients present with long, indolent course with progressive increase in joint pain
  - Joint pain (95%)
  - Fever (43%)
  - Periarticular swelling (38%)
  - Wound or cutaneous sinus drainage (32%)
- Presentation depends on virulence of causative microorganism

DIAGNOSIS OF PROSTHETIC JOINT INFECTIONS

- Need to differentiate infection from aseptic or mechanical problems
  - Infection – constant pain
  - Mechanical – pain with motion or weight-bearing
- Plain radiographs (findings in 50% of cases)
  - Abnormal lucencies at bone-cement interface
  - Changes in position of prosthesis components
  - Cement fractures
  - Periosteal reaction
  - Motion of components on stress views
DIAGNOSIS OF PROSTHETIC JOINT INFECTIONS

- Radioisotope scans
  - Increased technetium uptake seen around normal prostheses for 6 months after arthroplasty; positive scans after 6 months are abnormal, but do not necessarily indicate infection
  - Sequential gallium scanning is nondiagnostic because of unacceptable sensitivity and specificity
  - Indium-labeled leukocyte scanning is inconsistently sensitive and provides only nonspecific results
  - FDG-PET has reported low specificity (55%); more recently, 90% for hip and 75% for knee

- Isolation of pathogen by aspiration of joint fluid
  - Gram stain positive in 32%
  - Culture sensitivity 86-92%
  - Culture specificity 82-97%

- Culture of tissue at arthrotomy
  - Optimally obtain 5-6 specimens of tissue and fluid
  - 3 positive cultures – 94.8% probability of infection
  - No positive cultures – 3.4% probability of infection

MANAGEMENT OF PROSTHETIC JOINT INFECTIONS (2-STAGE)

- Removal of prosthesis and cement
- Use of methylmethacrylate cement spacer impregnated with antimicrobial agent (no controlled trials but commonly practiced)
- 4-6 weeks of bactericidal antimicrobial therapy
- Re-implantation at conclusion of antimicrobial therapy (?antimicrobial free period)
- Success 90-96% in hip replacement infections
- Success 97% in knee replacement infections

- Extraction with re-implantation after only 2 weeks of antimicrobial therapy, followed by additional 4 weeks of antimicrobial therapy (pathogen eradication in 79%; good function in 35%)
- Extraction of metallic joint and cement with immediate re-implantation of new prosthesis with antibiotic-loaded cement in 1-step procedure and antimicrobial therapy (success 70-83%)
- One-step procedure with infections caused by less virulent organisms and satisfactory condition of soft tissue (success 86-100%)

- Simple surgical drainage with prosthesis retention and antimicrobials (success 14-68%)
- Debridement with retention is reasonable, as follows:
  - Those with early postoperative or acute hematogenous infection
  - Clinical symptoms and signs <3 weeks (<1 week?)
  - Stable implant
  - Soft tissue in good condition; no sinus tract
  - Treat with effective agent for 3 months for infected hip prosthesis and 6 months for infected knee prosthesis
  - Success 82-100% for staph and 89% for strep

CASE #5

- 16-year old male steps on a nail which punctures his sneaker and enters his heel. Sees his physician who administers a tetanus booster and prescribes a 5-day course of amoxicillin/clavulanate
- Three weeks later has pain and purulent drainage from his right heel.
- On exam, T 100°F and purulent drainage from sinus track of right heel
- Cultures of drainage reveal S. aureus, E. coli, and E. faecalis
CASE #5

After appropriate bone cultures are obtained, which of the following antimicrobial regimens should be initiated?

A. Vancomycin + ceftriaxone
B. Vancomycin + metronidazole + ceftriaxone
C. Ampicillin/sulbactam + gentamicin
D. Vancomycin + piperacillin/tazobactam
E. Clindamycin + trimethoprim-sulfamethoxazole

EPIDEMIOLOGY AND ETIOLOGY OF CONTIGUOUS OSTEOMYELITIS

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Microorganism(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presence of foreign body</td>
<td>Coag-neg staph, S. aureus</td>
</tr>
<tr>
<td>Puncture injury to foot</td>
<td>P. aeruginosa</td>
</tr>
<tr>
<td>Malignant external otitis</td>
<td>P. aeruginosa</td>
</tr>
<tr>
<td>Periodontal infection</td>
<td>Oral flora, Actinomyces</td>
</tr>
<tr>
<td>Soil contamination</td>
<td>S. aureus, Clostridum, Enterobacteriaceae, Bacillus, Nocardia, atypical mycobacteria</td>
</tr>
</tbody>
</table>

EPIDEMIOLOGY AND ETIOLOGY OF HEMATogenous OSTEOMYELITIS

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Microorganism(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sickle cell disease</td>
<td>Salmonella, S. aureus, S. pneumoniae</td>
</tr>
<tr>
<td>IDU, hemodialysis</td>
<td>S. aureus, P. aeruginosa</td>
</tr>
<tr>
<td>Immunocompromised (including HIV)</td>
<td>Aspergillus, Candida, atypical mycobacteria, Bartonella henselae</td>
</tr>
</tbody>
</table>

GENERAL CONSIDERATIONS AND APPROACH TO OSTEOMYELITIS

- Pathogenesis may be hematogenous (monomicrobial), contiguous to a soft tissue infection (polymicrobial), or direct inoculation from surgery or trauma
- Conventional radiographs are inexpensive, with abnormalities seen in 10-14 days
- Nuclear bone scans are sensitive, but expensive and sometimes nonspecific
- MRI and CT are now considered standard of care, and are sensitive and specific in diagnosis

DIAGNOSTIC TESTS FOR OSTEOMYELITIS

<table>
<thead>
<tr>
<th>Test</th>
<th>Sen</th>
<th>Spec</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>3-phase bone scan</td>
<td>95%</td>
<td>33%</td>
<td>53%</td>
<td>95%</td>
</tr>
<tr>
<td>Gallium scan</td>
<td>81%</td>
<td>69%</td>
<td>71%</td>
<td>85%</td>
</tr>
<tr>
<td>Indium WBC scan</td>
<td>88%</td>
<td>85%</td>
<td>86%</td>
<td>87%</td>
</tr>
<tr>
<td>MRI</td>
<td>95%</td>
<td>88%</td>
<td>93%</td>
<td>92%</td>
</tr>
</tbody>
</table>
GENERAL CONSIDERATIONS AND APPROACH TO OSTEOMYELITIS

- Identification of causative microorganism is crucial to optimize medical therapy; if possible, withhold therapy until adequate cultures obtained
- Swab cultures from draining wounds and sinus tracts may be of value
  - Infection control for resistant microorganisms
  - Isolation of *S. aureus* correlates with deep infection
- Most infections require combined medical and surgical therapy for success
- Optimal duration of therapy is unknown (4-6 wks)

CASE #6

- 65-year-old man presented with hematuria; cystoscopy revealed a superficial transitional cell carcinoma of the bladder
- Treated with intravesicular therapy with successful resolution
- 2 months after completing therapy, presented with low-grade fever and moderate low back pain

VERTEBRAL OSTEOMYELITIS AND SPONDYLODISKITIS

- Hematogenous in most cases
- Clinical features
  - Localized insidious pain and tenderness (90%)
  - Fever (<50%)
- Etiology
  - *S. aureus* and coag-neg staph most common
  - Gram-negative bacilli and *Candida* in injection drug users, immunosuppressed, postoperative
  - Consider *Mycobacteria* and *Brucella* in appropriate clinical setting
- Diagnosis
  - MRI is gold standard; best for detecting disk space infection (98% sensitivity, 93% specificity)
  - Blood cultures
  - CT-guided percutaneous biopsy and aspiration off antibiotics (sensitivity 50%); repeat or do open biopsy if inconclusive

Which of the following is the most likely etiology of his vertebral lesions?

A. Enterococcus faecium
B. Pseudomonas aeruginosa
C. Mycobacterium bovis
D. Candida glabrata
E. Metastatic bladder cancer
VERTEBRAL OSTEOMYELITIS AND SPONDYLODISKITIS

- Management
  - Stabilize spine; surgery usually not needed
  - Antimicrobial therapy (6-8 weeks or longer)
  - If hardware present with early postop infection, debridement + long-term antimicrobial therapy (until evidence of bone vertebral fusion)
  - If hardware present with late postop infection, remove hardware + antimicrobial therapy
  - Follow-up ESR/CRP

OSTEOMYELITIS IN PATIENTS WITH DIABETES MELLITUS OR VASCULAR INSUFFICIENCY

- Foot is most commonly involved
- Probe to the bone test
  - Positive predictive value 89%
  - Negative predictive value 56%
- Revascularization in those with poor arterial vascular supply to provide flow to debrided area and minimize possible amputation

TESTS FOR OSTEOMYELITIS IN DIABETIC FOOT ULCERS

<table>
<thead>
<tr>
<th>Test</th>
<th>Sen</th>
<th>Spec</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probe to bone/exposed bone</td>
<td>60%</td>
<td>91%</td>
</tr>
<tr>
<td>Radiography</td>
<td>54%</td>
<td>68%</td>
</tr>
<tr>
<td>Bone scan</td>
<td>81%</td>
<td>28%</td>
</tr>
<tr>
<td>Leukocyte scan</td>
<td>74%</td>
<td>68%</td>
</tr>
<tr>
<td>MRI</td>
<td>90%</td>
<td>75%</td>
</tr>
</tbody>
</table>

OSTEOMYELITIS IN PATIENTS WITH DIABETES MELLITUS OR VASCULAR INSUFFICIENCY

- Management of dead space and adequate surgical drainage of soft tissue and bone
- Treatment failure often due to lack of adequate debridement
- Empiric antimicrobial therapy directed multiple aerobic and anaerobic microorganisms