

Bone and Joint Infections

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Objectives

- **Understand the causes, clinical features, and treatment of septic arthritis or native and prosthetic joints**
- **Understand the causes, clinical features, and treatment of osteomyelitis, with or without hardware**

Case

69 y/o diabetic man, recently immigrated from Vietnam to be with his kids, comes to establish care. He says he is healthy with no past medical issues. You note his BP is 180/110, he has cataracts in both eyes, has not had any immunizations, and is a smoker.

On your way to leave the room you happen to touch his shin looking for edema and note a bandage under his pants. When you look at it, you notice it is soaked with pus coming from what appears to be a sinus tract. On questioning, the patient says he was wounded during the war and this wound open and closes regularly over the years.

He denies any systemic symptoms and it only hurts right before it opens up to drain

Osteomyelitis

- Acute or chronic; hematogenous or non-hematogenous
- Acute: symptoms for days or weeks; sequestra are absent
- Chronic: months to years, sequestra are usually present. Sinus tracts may be present
- Hematogenous: spread of organisms through the blood
- Non-hematogenous: direct spread from a local source (skin/soft tissue or adjacent joints), or direct inoculation from surgery or trauma

Non-hematogenous Osteomyelitis

- In younger adults, this usually results from trauma or related to surgery
- In older adults, this usually results from spread from local infections, like diabetic foot wound or decubitus ulcers
- Risk factors include slow to heal chronic wounds, presence of orthopedic hardware, diabetes, peripheral vascular disease, neuropathy
- Microbiology is often polymicrobial, reflecting organisms at that site. But it is also often monomicrobial with *Staphylococcus* being the most common organism isolated.

Non-hematogenous Osteomyelitis

- Acute Osteomyelitis: gradual onset of symptoms of days to weeks; pain, local signs of inflammation, systemic symptoms. But can just be pain (especially when involving spine, pelvis, and hip)
- Chronic: onset over weeks to months; pain with swelling, redness; a sinus tract is often present. Ulcers that fail to heal with appropriate care, especially when overlying a bony prominence, and non-healing fractures may represent chronic osteomyelitis.
- Being able to probe to bone is often a marker of osteomyelitis. One study showed a sensitivity and specificity of 87 and 83%.
- Lab tests include elevated WBCs, ESR, CRP

Hematogenous Osteomyelitis

- Occurs mostly in children
- In adults, infection of the spine is the most common version, followed by flat bones of the axial skeleton (sternoclavicular or pelvic bones)
- In children long bones are most common
- Risk factors for adults include: endovascular infections, injection drug use, dialysis, sickle cell disease, and presence of orthopedic hardware
- Micro: usually *S. aureus*, and usually monomicrobial.

Complications of Osteomyelitis

- Sinus tract
- Contiguous soft tissue infection
- Septic arthritis
- Systemic infection (bacteremia)
- Bony deformity
- Fracture
- Malignancy



Work up

- If symptoms present >2 weeks, start with plain films
- If symptoms present <2 weeks, MRI or CT preferred
- If hardware precludes use of MRI or CT, nuclear medicine studies preferred
- In general, imaging consistent with osteomyelitis should prompt a bone biopsy for pathology and culture.
- Blood cultures can be done, especially if there are systemic symptoms
- Open biopsies are better than needle biopsies, to the point that in one study looking at diabetic foot cultures, concordance between bone and needle biopsies was 23%
- DNA testing for bacterial, fungal, and AFB

A note on imaging

- Plain films have a sensitivity of 22-75%, but can be negative for the first two weeks
- MRI has a sensitivity/specificity of 90/79%. It usually shows changes within 1-5 days. Contrast doesn't help with the bone, but does help in differentiating abscess, necrotic tissue and phlegmon. It also helps visualize sinus tracts. MRI changes can last for weeks to months following therapy
- CTs: better resolution than plain films
- Nuclear studies include: PET scan (sens/spec of 74 and 91% and may be best modality for chronic osteo), three phase bone scan (sens/spec with a normal x-ray 95%), tagged WBCs (similar to bone scan but can be less helpful in chronic osteo)
- Pitfalls: Charcot's , fractures, hardware, bone disease call all be misleading

Mimics

- Charcot arthropathy: hard to tell the difference on imaging, can also exist with osteomyelitis
- Avascular Necrosis of the Bone: usually can tell the difference by imaging, and often an antecedent cause is present (radiation, steroids, bisphosphonates)
- Gout: usually more acute, and of course crystals

Treatment: no hardware

Surgery: in general, dead bone will not be cured by antibiotics alone

Antibiotics:

- Empiric Therapy: vancomycin plus ceftriaxone or cefepime
- Targeted therapy based on the organism
- Duration is usually 6 weeks, based on the time it takes debrided bone has become covered by vascularized soft tissue
- If debridement has removed all infected bone, 10-14 days of antibiotics for the soft tissue per UpToDate, but I would say shorter course of 5-7 days

Treatment Hardware

Surgery: If possible, removal of hardware and debridement of dead bone

Antibiotics:

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When the hardware can't be removed

Antibiotics:

- Empiric Therapy: vancomycin plus ceftriaxone or cefepime
- Targeted therapy based on the organism
- For *S. aureus*, often add rifampin if it is susceptible
- Duration is usually 6 weeks parenteral therapy (again), but is controversial
- Often oral antibiotics are used after 6 weeks for variable amounts of time. Time limited to ensure healing of the bone. Forever if the patient couldn't tolerate removal of the hardware at a later date (and can tolerate the oral antibiotics).

But what about that article I saw in the NEJM?

Oral versus intravenous antibiotics for bone and joint infections. The OVIVA trial.

- UK study where 1054 patients were enrolled at 26 centers. Within 7 days of surgery or starting antibiotics, they were randomized into oral or intravenous antibiotics for 6 weeks. Oral antibiotics after that time were allowed in both groups. Oral antibiotics were non-inferior to intravenous antibiotics as defined by failure at 1 year.

Case

78 y/o diabetic woman with known diverticular disease causing colovesicular fistula, s/p diverting colostomy, RA, presented to the ED with fever, sepsis.

- Imaging showed presumed pelvic abscess, and she was admitted to the colorectal surgery service. Overnight, blood cultures grew MRSA.
- She continued to be bacteremic over the course of a week, getting initially vancomycin until the MIC came back at 2, then daptomycin. The pelvic collection was felt to be urine, not abscess.
- She developed wrist, hip, and low back pain. She had chronic low back pain s/p hardware that worsened over the course of her stay. Imaging showed spinal osteomyelitis and discitis with an epidural abscess.
- She was taken to surgery and debrided. It wasn't clear her hardware was involved, but rifampin was added. She improved and finally cleared her blood cultures, only to develop a surgical site infection.
- Antibiotics were broadened to include gram-negatives but the wound eventually dehiscd and she was taken back to the OR. Cultures grew MRSA again, now resistant to both daptomycin and rifampin.
- She finally settled down (for now) on ceftaroline.

Spinal Osteomyelitis/discitis

- Usually hematogenous in origin, although can result from direct inoculation from surgery, injections, or direct spread from contiguous soft tissues
- Usually occurs in adults, usually older than 50. M:F ratio 2:1 although why is not understood
- Risk factors include injection drug use, endovascular infections, dialysis, DJD of the spine, diabetes, steroids or immunocompromised status
- Infection can spread out causing epidural abscesses, paraspinal/psoas abscesses

Microbiology

- *S. aureus* is the most common organism, in 50%
- Various *Streptococci*, *Pseudomonas* next most common
- More rarely, TB, yeast, Brucellosis, *Salmonella*

Clinical Features:

- Pain at infected bone/disc site, aggravated by movement or palpation. Pain begins insidiously and worsens over weeks to months (but can be acute)
- Radiculopathy or neurologic signs can develop, especially when an epidural is present
- Fever often absent
- High ESR/CRP, abnormal imaging

Diagnosis and Treatment

- Spinal bone sampling, needle or open, for pathology and microbiology (consider PCRs)
- Blood cultures (if *S. aureus*, may not need bone sample)
- If first sample negative, but clinical suspicion remains high, sample again
- If the patient is not improving (clinically or by inflammatory markers) within 3-4 weeks, sample back again
- Duration of therapy is unclear. Minimum of 6 weeks, but for MRSA or other resistant organisms, 8 weeks. If extensive bone involvement, undrained abscesses, slow clinical response, we sometimes treat up to 12 weeks
- We do not routinely recheck imaging at the conclusion of therapy

Role for surgery

- Neurologic deficits
- Epidural or paravertebral abscess in need of drainage
- Threatened or actual cord compression due to collapse or spine instability
- Failure of antibiotics alone

Case

- 46 y/o presented to Yakima Memorial with 4 weeks of worsening mid back pain, worsened by his work at a factory. His exam was unremarkable and he was sent home with NSAIDs.
- 1 week later, he returns with worsening back pain, exam is the same, x-ray normal except for DJD, and he is sent out now with steroids in addition to his NSAIDs.
- 1 week later he returns with low grade fevers, worsening back pain, and an MRI shows spondylodiscitis.
- Further history reveals that he immigrated here from Ecuador 5 years ago and his mother had TB when he was a child.

Septic arthritis

- Infection either via hematogenous seeding or direct inoculation
- Microbiology: similar to bone infections, but with the addition of *N. gonorrhoeae* as a cause in young adults. So usually Staphylococcus, Streptococci, more rarely, gram-negatives, yeast, mycobacteria. Polymicrobial infection uncommon except in the case of penetrating trauma and bites
- Clinical features: acute pain, redness, swelling, DROM in one joint. Often have systemic symptoms like fever. Knee involved 50% of the time, with most others involving the wrists, ankles, and hips. Symphysis pubis or sternoclavicular joints sometimes in injection drug users. Involvement of multiple joints more common in RA patients or other rheumatologic disease

Septic arthritis

Lab:

- Leukocytosis
- High ESR/CRP
- Bacteremia in 50%
- Synovial fluid with high WBC count (50-100K) that is mostly neutrophils
- Positive Gram stain or culture from synovial fluid
- Crystals point against infection, but can be precipitated by infection

Imaging:

- Plain films, CT, MRI

Septic arthritis

Gonococcal Arthritis:

- Young sexually active adults
- Often febrile, mono- or oligoarticular disease
- Often with rash, polyarthralgias, tenosynovitis
- Often grows from blood, but will not grow on standard culture media. Lab needs to know you are worried about this from joint fluid (or routinely set up Chocolate or Thayer-Martin media for joints)
- Think CH50 testing for late complement deficiency

Lyme: consider with appropriate exposure and monoarticular arthritis; rash and systemic symptoms precede by weeks/months

Viral: Zika, Chikungunya, parvovirus, rubella

TB: will need special media

Septic arthritis: Treatment

Joint Drainage:

- Arthrotomy
- Arthroscopy
- Aspiration

Empiric antibiotics with negative Gram stain

- Normally, vancomycin
- Traumatic: vancomycin plus ceftriaxone
- Immunocompromised or IVDU: vancomycin plus cefepime
- Bites: Ampicillin-sulbactam; ceftriaxone plus metronidazole

Septic arthritis: Treatment

Duration of antibiotics is uncertain

- *S. aureus* with bacteremia, 4-6 weeks
- *S. aureus* w/o bacteremia, 2 weeks iv, 2 weeks po
- If high oral bioavailability antibiotics work: 1 week iv, 2 weeks po
- If *Pseudomonas* or *Enterobacter*: 3-4 weeks iv

- What are the high oral bioavailable antibiotics?
- Quinolones, TMP-SMX, metronidazole, doxycycline, clindamycin, rifampin, linezolid, fluconazole

Prosthetic Joint Infections: risk

- Risk greatest for knee and hip arthroplasty
- Risk highest in first 2 years following joint surgery
- RA, DM, malignancy, CKD, obesity, lymphedema, immunosuppression
- Prior arthroplasty or prior infection at the site
- ASA score >3
- Prolonged surgery
- Post-operative wound dehiscence or hematoma
- Bacteremia, especially *S. aureus*
- Tobacco or alcohol use

Prosthetic Joint Infections: microbiology

- Within 3 months of surgery: *S. aureus*, Gram negatives, anaerobes, polymicrobial
- 3-12 months: Coagulase-negative Staphylococci, *Cutibacterium acnes*, Enterococci
- >12 months: *S. aureus*, Gram negatives, Streptococci
- Cultures are negative in 7-39% of patients. Indolent infections are often more likely to be negative

Clinical Features

Signs/Symptoms

- No surprises here
- Painful, red, warm joint with DROM. May or may not have systemic symptoms
- If chronic, draining sinuses

Imaging: loosening of hardware on plain films the usual. Rarely CT/MRI (hardware-associated artifact often makes interpretation difficult)

Labs: cell/count/culture/crystals, ESR/CRP/IL-6?, OR Cultures (at least 3 specimens) and histopathology, sonication of explanted prosthesis. Blood cultures if fever.

- Synovial fluid alpha-defensin: FDA approves test is available, but it is unclear if it is more helpful than cell count and culture. It is supposed have sensitivity/specificity of 78/91%
- PCRs for bacterial, fungal, AFB DNA

Prosthetic joint infection treatment

Surgery and/or antibiotics

Surgery:

- Debridement and plastic exchange, retention of prosthesis: infection within 30 days of implant or <3 weeks of symptoms and a well-fixed prosthesis. Works in 70% of cases
- Explant with spacer or rarely in the US explant and reimplantation of a new prosthesis: loosened hardware or more chronic symptoms
- Permanent resection arthroplasty
- Amputation (yikes!)

Antibiotics

- Usually can wait till surgery done, but if empiric: vancomycin and cefepime
- If prosthesis is retained: 2-6 weeks iv antibiotics, followed by longer oral. 6 months total therapy for knees, 3 for all other joints. If *S. aureus* and rifampin is susceptible, we usually add rifampin for the first 6 weeks.
- If prosthesis is explanted: 6 weeks iv antibiotics but no need for a longer oral course. 2 weeks after stopping antibiotics, re-evaluate for clinical signs/symptoms or worsening, check ESR/CRP, some will attempt to aspirate the knee.