50 – Bone and Joint Infections

Speaker: Sandra Nelson, MD

IDBR INFECTIOUS DISEASE BOARD REVIEW AUGUST 20-24 2022

Bone, Joint and Musculoskeletal Infections

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Disclosures of Financial Relationships with Relevant Commercial Interests

- None

Osteomyelitis:

- Hematogenous Osteomyelitis
  - Metaphyseal long bone (more common in children)
  - Vertebral spine (Spondylodiscitis)
  - Usually monomicrobial
- Contiguous Osteomyelitis
  - Trauma / osteofixation
  - Diabetic foot ulceration
  - Infections in decubitus ulcer
  - Often polymicrobial

Osteomyelitis: Unifying Principles

- Radiographic studies:
  - No radiographic study sufficiently specific to confirm diagnosis of osteomyelitis
  - MRI is the most sensitive radiographic study for diagnosis
  - Serial plain films and CT may also be useful in subacute and chronic infection
  - Bone scan has high negative predictive value but lacks specificity
  - No radiographic studies useful as test of cure
- Diagnosis best confirmed by bone histopathology and culture
  - Identification of organism improves outcomes
  - Swab cultures of drainage are of limited value
- Optimal route and duration of therapy an evolving target
  - 6 weeks of IV antimicrobial therapy commonly employed; strong data to support oral therapy
  - Longer oral suppression in setting of retained hardware

Brodie's Abscess (Subacute hematogenous osteomyelitis)

- More common in children and young adults
- Bacteria deposit in medullary canal of metaphyseal bone, become surrounded by rim of sclerotic bone → intraosseous abscess
- "Penumbra sign" on MRI
  - Granulation tissue lining abscess cavity inside bone gives appearance of double line
- *Staph aureus* most common

Simpfendorfer Infect Dis Clin N Am 2017;31:299

Case #1

- 57-year-old male presented with 3 months of progressive lower back pain
- On ROS denied fevers or chills but wife noticed weight loss
- Originally from Cambodia, emigrated as a child.
- Employed at a seafood processing plant
- ESR 84 CRP 16
- MRI with discitis and osteomyelitis at L5-S1
- Blood cultures grew *Staph epidermidis* in 2 of 4 bottles

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Case #1: Vote

What is the best next step in management?

A. Repeat 2 sets of blood cultures
B. Initiate vancomycin; place PICC for six week treatment course
C. Obtain interferon gamma release assay
D. Percutaneous biopsy of disc space
E. Empiric treatment with rifampin, isoniazid, ethambutol, and pyrazinamide

Pyogenic Vertebral Osteomyelitis: diagnosis

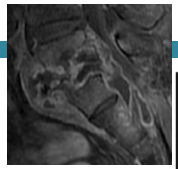
- Plain films and CT useful in subacute to chronic infection
  - Loss of disc height, endplate sclerosis
  - Can look similar to degenerative disease
- MRI best imaging test in early infection
  - Disc hyperintensity and loss of disc height
  - Marrow edema
  - Contrast enhancement
  - Erosive changes involving endplates
  - Associated paraspinal and/or epidural collections
  - Infection: almost always involves two contiguous vertebral bodies

Pyogenic Vertebral Osteomyelitis: diagnosis

- Blood cultures (positive in 60%)
  - No further diagnostics if *Staph aureus* or *Staph lugdunensis*
- Brucella serologies, PPD/IGRA
  - In appropriate epidemiological setting
- Percutaneous biopsy (paraspinal or bone/disc)
  - When blood cultures and serology negative
  - Yield 36-65%
  - In absence of sepsis and/or neurologic compromise, withhold antibiotics 1-2 weeks if feasible
  - If negative repeat percutaneous or consider open procedure (higher yield)

Reference: 2015 IDSA Guidelines

Pott's Disease



- Clinically:
  - More indolent than pyogenic osteomyelitis
  - Constitutional symptoms common
  - Anterior collapse may lead to gibbus deformity
- Radiographic:
  - Thoracic>lumbar with anterior involvement
  - Relative sparing of the disc space until later
  - Multi-level disease, large paraspinal abscesses
- Treatment:
  - Conventional TB therapy, 6-12 months
  - Surgery often not necessary

Simpfendorfer Infect Dis Clin N Am 2017;31:299

Septic Arthritis

Septic Arthritis: Clinical Pearls

- Synovial fluid cell counts: No diagnostic threshold
  - Higher probability of SA if WBC >50,000/mm^3
  - Lower cell counts do not exclude septic arthritis
- More subtle presentations in immunocompromised hosts and with indolent organisms
  - Subacute history
  - Lower synovial fluid cell counts
- Negative cultures and/or delayed culture positivity:
  - think Gonococcus, HACEK, Lyme, Mycoplasma
- Surgery indicated for most patients with joint sepsis
  - Type of surgery not standardized

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Polyarthritis

- 10-20 % of septic arthritis is polyarticular:
- Associated with bacteremia/sepsis
  - Staph aureus most common (look for endocarditis)
- Consider also:
  - gonococcal, viral, non-infectious
- Rat bite fever
  - Polyarthritis (usually symmetric), fever, maculopapular and/or pustular rash
  - *Streptobacillus moniliformis* (or if bitten in Asia – *Spirillum minus)*
  - Rx: penicillin

Giorgiutti NEJM 2019: 381:1762

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Gonococcal Arthritis

- Tenosynovitis, arthralgias, skin lesions
  - Especially extensor surface tenosynovitis
  - Migratory arthralgias
- Purulent arthritis
  - May be polyarticular; knees most common
  - Lower synovial fluid cell counts more common
- Asymptomatic mucosal phase predisposes
  - Dissemination more common in women
- Highest yield diagnosis: mucosal site sampling (cervical, urethral)
  - Blood (<30%) and synovial fluid (<50%) cultures lower yield
  - Compatible clinical syndrome

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Viral arthritides

- Symmetric polyarthritis, often involving small joints, often associated with fever and rash
- Diagnose serologically (+IgM or 4 fold rise in IgG titer)

Most common viruses to cause arthritis	Clinical and Epidemiologic Clues
Parvovirus B19	More common in women. History of exposure to young children, often a teacher or parent. Hands most common; can be severe.
Rubella	Non-immune (non US born). See cervical lymphadenopathy, fever, rash.
Hepatitis B Virus	Serum-sickness like reaction, resolves with development of jaundice; also polyarteritis nodosa (PAN)
Hepatitis C Virus	Immune complex arthritis associated with cryoglobulinemia
Alphaviruses (esp Chikungunya)	Travel to endemic areas

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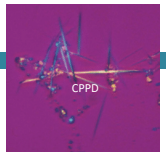
Crystalline arthritis: clinical pearls



- Acute gout flare mimics septic arthritis
  - Fever common
  - Monoarthritis and polyarthritis forms
  - Clues: rapid onset (hours), history of prior gout, alcohol, CKD, diuretics, elevated uric acid
  - Synovial WBC 10,000-100,000/mm^3
- Crystalline disease and septic arthritis can coexist (esp. CPPD)
  - CPPD rarely has cell count >30,000
  - CPPD rarely associated with high fever

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Masquerading as Infection…

- Other noninfectious causes of arthritis:
  - Reactive arthritis
    - Following enteric or genitourinary infection
    - Asymmetric mono or oligo-arthritis affecting knees/ankles
    - Associated features: enthesitis (tendon insertion), dactylitis (sausage digits), mucosal lesions, urethritis, conjunctivitis/uveitis, skin lesions (keratoderma blennorhagica)
  - Still's disease
  - Sarcoid (Lofgren's)
  - Polymyalgia rheumatica
  - Many others….

Coelho BMJ Case Reports 2017-222475

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Osteofixation Infections

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Case #2

- 44-year-old healthy woman suffered a right ankle closed pilon fracture and underwent open reduction and internal fixation (ORIF)
- Chronically discharging wound despite courses of cephalexin and trimethoprim-sulfamethoxazole
- Two months after ORIF, superficial wound culture grows methicillin-susceptible *Staph aureus*
- Plain films: Hardware intact; fracture not yet consolidated

Case #2: Vote

What are your next steps?

A. Nafcillin followed by long-term trimethoprim- sulfamethoxazole
B. Hardware removal; six weeks of oxacillin
C. Hardware removal; six weeks of oxacillin and rifampin
D. Debridement without hardware removal; six weeks of oxacillin and rifampin
E. Debridement and hardware replacement; six weeks of oxacillin and rifampin

Osteofixation Infections

Goals: fracture consolidation and infection eradication
Removal of hardware depends upon fracture healing

	Early or delayed infections prior to fracture union	Late nonunion	Late, healed fracture
Microbiology	*Staph aureus* most common Virulent organisms	Indolent organisms (coagulase-negative Staphylococcus, *Cutibacterium acnes*)	Often indolent organisms, or recurrence of early infection
Surgical Strategy	Debride and retain (assuming implants well fixed)	Hardware removal Revision fixation (1 or 2 stage) Or external fixation	Hardware removal
Antimicrobial Management	Pathogen-directed therapy with addition of rifampin if Staph species. Duration not well studied, often 12 weeks or until fracture consolidation	Pathogen-directed therapy Duration not well studied	Pathogen-directed therapy Duration not well studied; two weeks following hardware removal

Rifampin in orthopedic infections

- Considered a "biofilm active" agent
- Best studied for Staphylococcal PJI in setting of hardware retention
  - Data extrapolated for other hardware infections (osteofixation, spinal implant)
  - Lower treatment failure in PJI with implant retention
- Specifics
  - Never to be used in monotherapy of established infection
  - Should not be used prior to surgical debridement and until partner drug therapeutic
  - Multiple drug interactions (primarily via Cyp 3A4 pathway)

Prosthetic Joint Infection

Prosthetic Joint Infection (PJI): Clinical presentations

- Early surgical site infection (< 3months)
  - Acute onset of fever, joint pain, swelling
  - Caused by virulent organisms (*Staph aureus*)
- Delayed / Subacute infection (3 – 24 months)
  - Insidious onset of pain; fever is uncommon
  - Less virulent organisms: e.g. Coagulase-negative Staph, Cutibacterium
- Acute hematogenous infection (anytime after arthroplasty)
  - Acute onset fever, joint pain, swelling in previously well joint replacement
  - Hematogenous seeding, virulent organisms (*Staph aureus, Streptococcus)*

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Prosthetic Joint Infection: Diagnostic pearls

- Diagnosis of acute PJI usually straightforward
- Multiple diagnostic algorithms have been developed for chronic PJI
  Diagnosis of chronic PJI confirmed if:
  - Sinus tract to the joint
  - Two synovial fluid or tissue cultures positive with the same organism

	Early PJI and Late hematogenous	Delayed (chronic) PJI
ESR/CRP	High	May be normal or moderately elevated
Plain films	May be normal; effusion	May be normal or show periprosthetic lucency
Synovial fluid	WBC > 10,000/μL % pmns > 90	WBC > 3000/μL % pmns > 70

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PJI Management

Surgical Procedure	Most appropriate for:	Antimicrobial Therapy*
Debridement and implant retention (exchange of polyethylene liner)	Acute infections - both early and late Well-fixed components	2-6 weeks IV antibiotics 3-6 months oral antibiotics Rifampin if Staph
1 stage exchange	Acute and subacute infections with healthy soft tissues, sensitive organisms	2-6 weeks IV antibiotics 3-6 months oral antibiotics Rifampin if Staph
2 stage exchange "Spacer" utilizing antibiotics in cement	Chronic infections Sinus tracts Resistant organisms	6 weeks IV or highly bioavailable oral antibiotics

* 2012 IDSA Guidelines

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Case #3

- A 57-year-old woman underwent total hip arthroplasty
  - She never achieved a pain-free state after surgery
- Eighteen months postoperatively, she was diagnosed with delayed periprosthetic infection due to *Enterococcus faecalis*
  - Sensitive to ampicillin, vancomycin, linezolid, daptomycin, gentamicin
- Her orthopedist plans a two-stage exchange procedure utilizing a temporary spacer comprised of polymethylmethacrylate (PMMA)

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Case #3: Vote

You are asked to provide recommendations about systemic and local antimicrobial therapy for the spacer. She has no antimicrobial allergies. You advise:

A. Ampicillin in the cement; systemic vancomycin
B. Ampicillin in the cement; systemic ampicillin
C. Gentamicin in the cement; systemic ampicillin
D. Tobramycin in the cement; systemic daptomycin
E. Ceftriaxone in the cement; systemic linezolid

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Antimicrobial Cement (PMMA)

- Mechanical function "spacer":
  - Joint stability, allows mobility, prevents contractures, facilitates reoperation
- Elution: high levels within the first few days
  - Local tissue concentration exceeds systemic delivery
  - May elute for months or longer
- Antimicrobial considerations
  - Known or suspected organisms
  - Thermal stability (avoid most β-lactams)
  - Osteocyte toxicity (avoid quinolones)
  - Vancomycin and aminoglycosides most common
  - Toxicity and allergy reported but rare

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Case #4

- A 63-year-old woman with rheumatoid arthritis is anticipating knee arthroplasty. She takes methotrexate, hydroxychloroquine and low dose prednisone (2.5 mg daily). She has a history of recurrent urinary tract infections. She asks how she might prevent infection after knee replacement.

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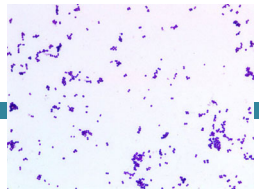
Case #4: Vote

What do you advise?

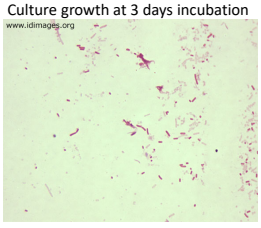
A. Stop methotrexate and prednisone two weeks preoperatively
B. Screen for Staph aureus colonization; decolonize if present
C. Screening UA and urine culture, treat if positive
D. 48 hours perioperative prophylaxis with cefazolin
E. Amoxicillin prior to dental procedures for 2 years postoperatively

Microbiology of Musculoskeletal Infections



Case #5: Vote

Culture growth at 3 days incubation



What is the most likely organism?

A. *Serratia marcescens*
B. *Salmonella heidelberg*
C. *Staphylococcus aureus*
D. *Kingella kingae*
E. *Pasteurella multocida*

Prevention of PJI

- Immunosuppressives:
  - Stop biologics, no need to stop DMARDs or low dose prednisone
- Surgical antibiotic prophylaxis: one dose prior to surgery
- Urinary tract infections:
  - Diagnose and treat symptomatic UTI
  - Do not screen for asymptomatic bacteriuria
- Dental prophylaxis: no more!
- *Staph aureus* decolonization reduces surgical site infection

Case #5

56-year-old man presents to ED with a one-week history of atraumatic right knee pain and swelling and low-grade fevers. Weight bearing is now uncomfortable.

- PMHx: poorly controlled diabetes
- One month ago he travelled to the Dominican Republic
  - No illnesses while traveling
- He last saw a dentist six months ago; no tooth pain
- No animal exposures
- No history of injection drug use
- Exam: moderate effusion; pain with passive range of motion
- ESR 68 CRP 17 mg/dL
- Synovial fluid: 45,000 WBCs (82% neutrophils)
  - Negative gram stain

Microbiology of Bone and Joint Infections: clinical and epidemiologic clues (1)

Gram-negative Organisms	Clinical Clues	Micro Clues
Pseudomonas aeruginosa and Serratia marcescens	Immunocompromised host, indwelling line, history of injection drug use (IDU)	
HACEK organisms	Human bite wounds (*Eikenella corrodens*) Recent dental procedure or infection	Delayed growth in culture Often culture negative if prior abx
Kingella kingae (K in HACEK)	Common in children <4yo.	Grows poorly in routine culture (diagnose by pcr)
Pasteurella species	Cat or dog bite; rapid onset infection	
Salmonella species	Sickle cell disease, immunocompromise, diabetes. Reptile exposure. Travel to developing world or unsafe food hygiene	
Brucella species	Consumption of unpasteurized dairy; travel to endemic areas (Latin America, Mediterranean Middle East). Sacroiliitis and spondylodiscitis	Delayed growth in culture Can be a biohazard in the laboratory
Streptobacillus moniliformis	Rat bite Fever, rash, polyarthritis	

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Microbiology of Bone and Joint Infections: clinical and epidemiologic clues (2)

Other bacteria and mycobacteria	Clinical Clues	Micro Clues
Neisseria gonorrhoeae	Triad of Tenosynovitis, Dermatitis, Arthritis	Requires enriched media (Thayer-Martin) to grow
Mycoplasma species	Humoral immunodeficiency (CVID, XLA) Postpartum women	Difficult to grow in routine culture. "Fried egg" morphology in culture
Borrelia burgdorferi (Lyme)	Northeast and Upper Midwest with tick exposure. Subacute monoarthritis of large joints (knee most common) with large effusions	Does not grow in conventional culture
Tuberculosis	Subacute to chronic infections including vertebral osteomyelitis (Pott's) and septic arthritis	
Non-tuberculous mycobacteria	Environmental water exposure (fishermen, fish tanks). Tenosynovitis of hands	

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Microbiology of Bone and Joint Infections: clinical and epidemiologic clues (3)

Fungal Infections	Clinical Clues
Candida species	Seen in immunocompromised hosts, IDU
Molds	Madura Foot (barefoot walking) Environmental contamination (e.g. open fracture with soil contamination) Immunocompromised hosts (neutropenia)
Coccidioides species, Blastomyces dermatitidis (Histoplasma capsulatum less frequent)	Subacute to chronic monoarthritis, long bone osteomyelitis, and vertebral disease. Usually associated with symptomatic or asymptomatic pulmonary findings (esp. cocci). Immunocompromised host

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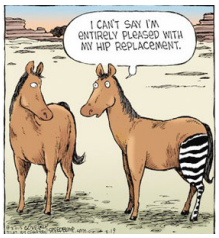
Thank you!



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