06 - Bone, Joint and Musculoskeletal Infections

Speaker: Sandra Nelson, MD

2020 INFECTIOUS DISEASE BOARD REVIEW

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
  - Often polymicrobial

Osteomyelitis: General Principles

- MRI and CT are the best radiographic studies
  - Bone scan has good negative predictive value but lacks specificity
  - MRI and CT not 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
  - Longer oral suppression considered 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 a 3 month history 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

- 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 space)
  - 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 (open procedure higher yield)

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

Polyarthritis

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

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

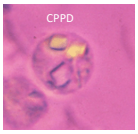
Viral arthritides

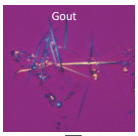
- Symmetric polyarthritis, often involving small joints, often associated with fever and rash
- Diagnose serologically (+IgM or 4 fold rise in IgG titer)

Most common viruses to cause arthritis	Clinical and Epidemiologic Clues
Rubella	Non-immune (non US born). See cervical lymphadenopathy, fever, rash.
Parvovirus B19	More common in women. History of exposure to young children, often a teacher or parent. Hands most common; can be severe.
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

Crystalline arthritis: clinical pearls

- Acute gout flare mimics septic arthritis (fever)
  - Clues: rapid onset (hours), history of 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





Images: Taljanovic RadioGraphics 2015;35:2026

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

Osteofixation Infections

Case #2

- 44 year old woman, previously healthy, suffered a right ankle closed pilon fracture
  - Open reduction and internal fixation
- Impaired wound healing
  - Chronically discharging wound despite courses of cephalexin and trimethoprim-sulfamethoxazole
- 3 months after ORIF, wound culture grows methicillin-susceptible *Staph aureus*

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

- Infection risk as high as 25% and varies based on:
  - Open fractures (type and inoculum of bacterial contamination)
  - Severity of fracture (Gustilo grade)
  - Severity of soft tissue injury
  - Fracture location (lower extremity higher risk)
  - Timely antibiotic prophylaxis for open fractures
  - Usual host risk factors

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
Microbiology	*Staph aureus* most common	Indolent organisms (coagulase-negative Staphylococcus, *Cutibacterium acnes*)
Surgical Strategy	Debride and retain (assuming implants well fixed)	Hardware removal Revision fixation (1 or 2 stage) Or external fixation
Antimicrobial Management	Pathogen-directed therapy Add rifampin if Staph species Consider suppression until fracture consolidates, especially if *Staph aureus*	Pathogen-directed therapy

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
  - Acute onset of fever, joint pain, swelling in previously healed and pain-free joint
  - Hematogenous seeding, virulent organisms (*Staph aureus, Streptococcus)*

Chronic PJI: diagnostic pearls

- ESR/CRP may be minimally elevated
- Plain films often normal or may show periprosthetic lucency
- Synovial fluid aspiration the best test
  - Lower cell counts than in native joints or acute PJI (> 3000 WBCs per µL)
  - Yield of synovial fluid culture 50-60%
    - » Reduced by prior antibiotics
  - Coagulase-negative Staph can be considered pathogenic if in >1 culture and compatible cell counts

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Case #3

- A 57 year old woman with a history of diabetes, hypothyroidism, and anxiety has undergone total hip replacement. Three weeks postoperatively, she developed erythema, swelling, and incisional drainage. She was taken back to the operative room, where she was found to have purulent infection within the joint pseudocapsule. The polyethylene liner was exchanged but acetabular and femoral components were secure and maintained in place. Operative cultures have grown methicillin-sensitive Staph aureus.

Case #3: Vote

You are asked to provide recommendations about antimicrobial management

A. Nafcillin for six weeks
B. Cefazolin and rifampin for six weeks
C. Cefazolin for four weeks followed by minocycline for two months
D. Cefazolin and rifampin for four weeks followed by minocycline and rifampin for two months
E. Vancomycin for six weeks followed by doxycycline for six months

PJI Management

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

*3 months for hips; 6 months for knees

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.

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

Prevention of PJI

- Immunosuppressives:
  - Stop TNF agents, 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; no role to screen for asymptomatic bacteriuria
- Dental prophylaxis: No more!
- *Staph aureus* decolonization reduces surgical site infection

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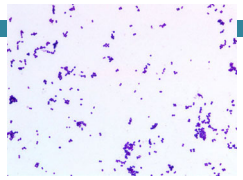
Microbiology of Musculoskeletal Infections

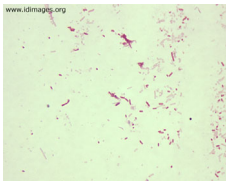


Case #5

- 56 year old man presents to ED with 1-2 week history of atraumatic right knee pain and swelling and low grade fevers; weight bearing is now very uncomfortable.
- He has poorly controlled diabetes. One month ago he travelled to the Dominican Republic where he swam in the ocean, recalls receiving several insect bites. He owns a pet kitten, last saw a dentist three months ago, and denies injection drug use.
- On exam, he has pain with passive range of motion and a moderate effusion.
- ESR 68 CRP 17 mg/dL
  Synovial fluid: 45,000 WBCs (82% neutrophils)
  Negative gram stain

Case #5: Vote

Culture growth at 3 days incubation



What is the most likely organism?

A. *Stenotrophomonas maltophilia*
B. *Salmonella heidelberg*
C. *Staphylococcus aureus*
D. *Kingella kingae*
E. *Pasteurella canis*

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

Gram Negative Organisms	Clinical Clues
Pseudomonas aeruginosa	Immunocompromised host, indwelling line, history of injection drug use (IDU)
HACEK organisms	Human bite wounds (*Eikenella corrodens*) Recent dental procedure or infection
Kingella kingae (K in HACEK)	Common in children <4yo. Grows poorly in routine culture (diagnose by pcr)
Pasteurella species	Cat or dog bite
Salmonella species	Sickle cell disease, diabetes, immunocompromise. Reptile exposure. Travel to developing world or unsafe food hygiene. +/- antecedent GI illness
Brucella species	Consumption of unpasteurized dairy; travel to endemic areas (Latin America, Mediterranean and Middle East). Sacroiliitis and spondylodiscitis
Streptobacillus moniliformis	Rat bite

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

Other bacteria and mycobacteria	Clinical Clues
Neisseria gonorrhoeae	Triad of Tenosynovitis, Dermatitis, Arthritis.
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.
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

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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