

21 – Bone and Joint Infections

Speaker: Sandra Nelson, MD



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



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Osteomyelitis: Unifying Principles

- MRI and CT are the best radiographic studies
 - Bone scan has high 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 in setting of retained hardware



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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



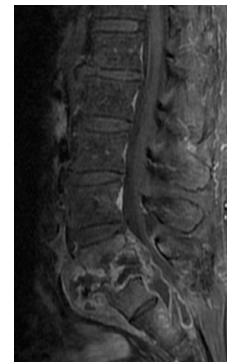
Simpfendorfer Infect Dis Clin N Am 2017;31:299



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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

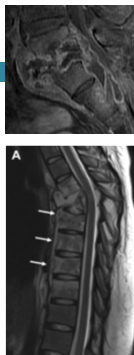
Pyogenic Vertebral Osteomyelitis: diagnosis



- 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
 - Infection: almost always involves two contiguous vertebral bodies

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



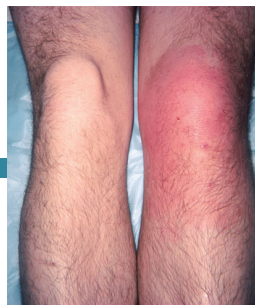
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Pyogenic Vertebral Osteomyelitis: diagnosis



- 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)

Septic Arthritis



Septic Arthritis: Clinical Pearls

- Synovial fluid cell counts: No diagnostic threshold
 - Higher probability of SA if WBC >50,000/mm³
 - 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*

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Polyarthrititis

- 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)
 - Polyarthrititis, 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



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Viral arthritides

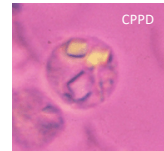
- Symmetric polyarthrititis, often involving small joints, often associated with fever and rash
- Diagnose serologically (+IgM or 4 fold rise in IgG titer)

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 polyarthritis 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/mm³
- Crystalline disease and septic arthritis can coexist (esp. CPPD)
 - CPPD rarely has cell count >30,000



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Images: Taljanovic RadioGraphics 2015;35:2026

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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 blennorrhagica)
 - Still's disease
 - Sarcoid (Lofgren's)
 - Polymyalgia rheumatica
 - Many others....



Coeelho 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



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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

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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

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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	<i>Staph aureus</i> most common Virulent organisms	Indolent organisms (coagulase-negative <i>Staphylococcus</i> , <i>Cutibacterium acnes</i>)
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 Consider rifampin if <i>Staph</i> species Consider suppression until fracture consolidates, especially if <i>Staph aureus</i>	Pathogen-directed therapy Duration not well studied

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Prosthetic Joint Infection



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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/ μ L % pmns > 90	WBC > 3000/ μ L % pmns > 70

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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:

- Ampicillin in the cement; systemic vancomycin
- Ampicillin in the cement; systemic ampicillin
- Gentamicin in the cement; systemic ampicillin
- Tobramycin in the cement; systemic daptomycin
- Ceftriaxone in the cement; systemic linezolid

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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

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* 2012 IDSA Guidelines

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Antimicrobial Cement (PMMA)

- Mechanical function "spacer":
 - Joint stability, allows mobility, prevents contractures, facilitates reoperation
- 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
- Elution: high levels within the first few days
 - Local tissue concentration exceeds systemic delivery
 - May elute for months or longer



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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

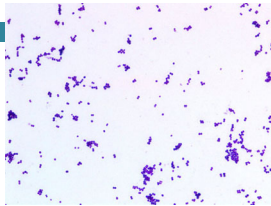
What do you advise?

- 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

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;
 - Do not screen for asymptomatic bacteriuria
- Dental prophylaxis: no more!
- *Staph aureus* decolonization reduces surgical site infection

Microbiology of Musculoskeletal Infections

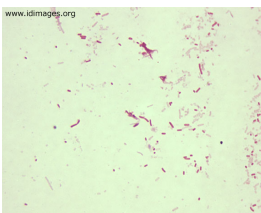


Case #5

- 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
 - Swam in pools, fished in the ocean
 - No illnesses while traveling
- He last saw a dentist six months ago; no tooth pain
- 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

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*

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

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

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

Other bacteria and mycobacteria	Clinical Clues
<i>Neisseria gonorrhoeae</i>	Triad of Tenosynovitis, Dermatitis, Arthritis.
Mycoplasma species	Humoral immunodeficiency (CVID, XLA) Postpartum women. Difficult to grow in routine culture. "Fried egg" morphology in culture
<i>Borrelia burgdorferi</i> (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)
<i>Coccidioides</i> species, <i>Blastomyces dermatitidis</i> (<i>Histoplasma capsulatum</i> less frequent)	Subacute to chronic monoarthritis, long bone osteomyelitis, and vertebral disease. Usually associated with symptomatic or asymptomatic pulmonary findings (esp. cocci). Immunocompromised host

Thank you!

