

Infectious Diseases

Lesson 10

OSTEOMYELITIS, PROSTHETIC JOINT INFECTIONS, DIABETIC FOOT INFECTIONS, AND SEPTIC ARTHRITIS

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Objectives, learning goal and contents

Objective

To review all relevant knowledge on infections affecting joints and bone

Learning goal

To acquire enough knowledge to properly manage a patient who presents with bone or joint infection in any clinical setting

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- [Osteomyelitis](#)
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Osteomyelitis

General concepts

- Definition: progressive infectious process that can involve one or multiple components of bone: periosteum, medullary cavity, and cortical bone
- Characterized by progressive **inflammatory destruction** of bone, by **necrosis**, and by **new bone formation**

Classifications, according to...

- Temporal profile
- Pathogenesis
- Affected area
- Extent of involvement
- Classifications guide prognosis and therapy

Classifications: temporal profile

- **Acute**, days to weeks
- **Chronic**, weeks to years; characterized by necrotic bone (sequestra), foreign material, and fistulous tracts

Classifications: pathogenesis

- **Hematogenous**, in prepubertal children and elderly
- Secondary to **contiguous focus**, follows trauma, perforation, or orthopedic procedure; **diabetic foot infection**: ulcer → bone; neuropathy and vascular insufficiency pathogenically relevant

Classifications: affected area

- **Medullary**, confined to the intramedullary surfaces of bone; hematogenous or infected intramedullary rods; may be cured with antibiotics alone
- **Superficial**, when bone lies at the base of a soft tissue infection; modality of “contiguous”; requires debridement

Classifications: extent of involvement

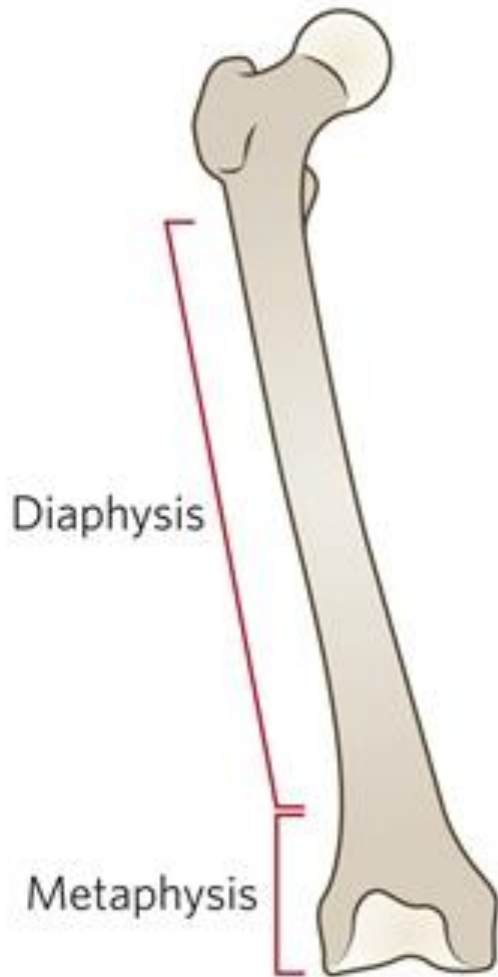
- **Localized**, discrete area of bone infection that may extend to the full thickness of the bone and may contain **cortical sequestration**, but can be surgically removed without impairing bony stability
- **Diffuse**, involves all regions of the bone and requires resection to arrest the spread of infection; bone stability is compromised either before or after debridement

Hematogenous osteomyelitis of long bones and vertebral bodies

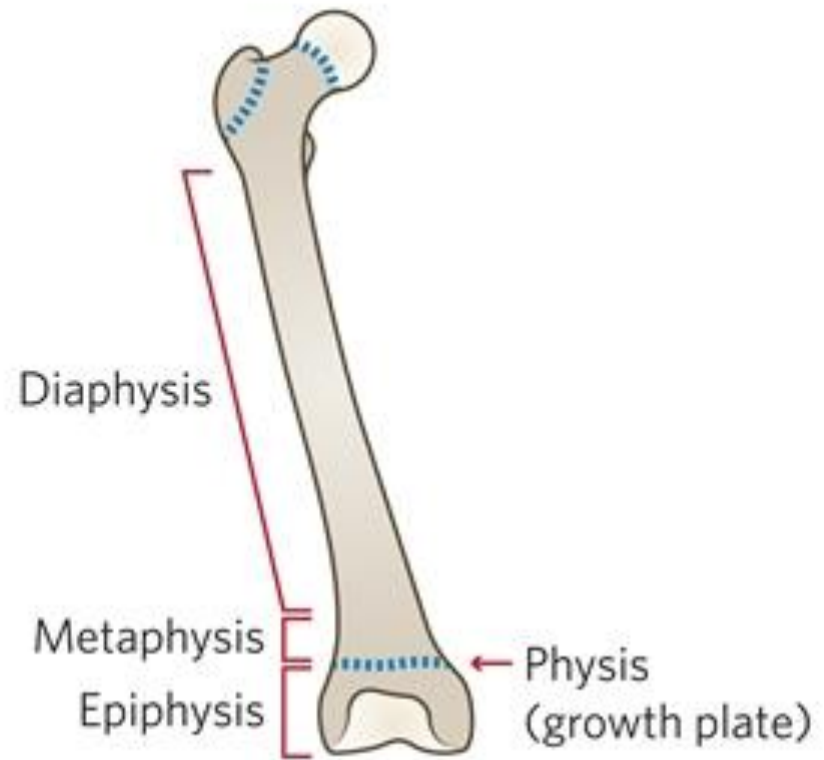
Pathogenesis

- **Children**, usually a single focus in the metaphysis of long bones (tibia, femur, etc.), bacteria lodge in small end vessels that form sharp loops near the epiphyses
- **Adults**, most frequently involves the vertebral bodies:
 - Via vertebral arteries that bifurcate and supply two adjacent vertebral bodies, so vertebral osteomyelitis involves two adjacent bony segments and intervening disc
 - Via Batson's plexus of veins that surrounds the vertebra and drains the bladder and pelvic region

Adult



Child



Microbiology

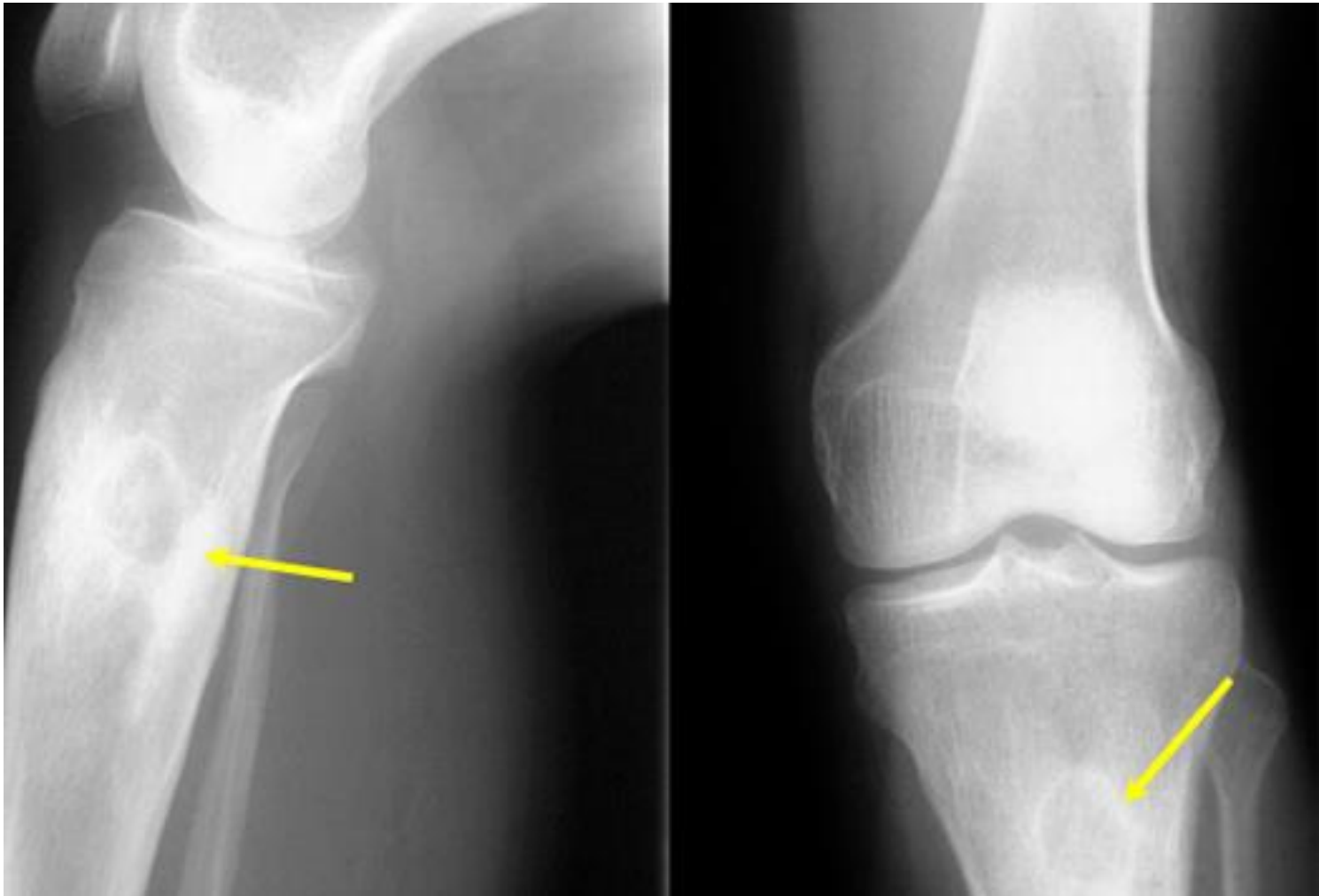
- Neonates include:
 - *Staphylococcus aureus*
 - *Escherichia coli*
 - Other gram negative rods
 - Group B streptococci
- Children and adults:
 - *S. aureus* predominates
 - **Many other** gram positive and gram negative bacteria, etc.

Clinical manifestations

- Chills, fever, and malaise
- Pain and local swelling at the site of infection
- Vertebral osteomyelitis:
 - Localized back pain, similar to degenerative diseases
 - Fever not always present, particularly in more chronic cases
- Blood analyses:
 - ↑ acute phase reactants
 - White blood cells count is frequently normal
 - If prolonged infection, normochromic normocytic anemia

Diagnosis - I

- Standard bone films:
 - Demineralization within 2-3 weeks of infection onset (in vertebrae 6-8 weeks); loss of 50% of bone calcium is generally required to be detected
 - **Lytic** lesions (\downarrow Ca) \rightarrow **sclerotic** lesions (\uparrow Ca)
 - Soft tissue swelling; periosteal elevation
 - Bone plate of the vertebra eroded \rightarrow collapse of disc
- Computed tomography (CT) scan: more reliable than standard bone films, useful to guide biopsy or surgery



Single focus of osteomyelitis in tibia metaphysis



Single focus of osteomyelitis in radius

Diagnosis - II

- **Magnetic resonance imaging (MRI):**
 - Useful to detect sequestra
 - Unique signal of bone marrow necrosis
 - Very effective to guide surgery
 - More sensitive than CT scan for detecting early osteomyelitis
 - ↓ signal intensity on T2, loss of endplate definition on T1 images
 - Contrast enhancement of the infected regions
 - Spread of vertebral infection to epidural space, etc.
- Tc, Ga bone scans not as useful as MRI



Discitis, vertebral osteomyelitis, spine instability and spinal cord compression



Discitis, vertebral
osteomyelitis and
spinal cord
compression



Discitis, and vertebral
osteomyelitis, and
paravertebral abscess

Diagnosis - III

- *Brucella* spp. serology in endemic areas
- Blood cultures, if negative → **deep** tissue sample: CT-guided needle biopsy → open biopsy:
 - Gram stain
 - Culture: **aerobic, anaerobic**, fungal, and mycobacterial
 - Histopathologic examination

Diagnosis - IV

- Simple needle aspiration or swabbed sample **useless**
- **Children** are often treated **empirically**, because procedures near the epiphyseal plate can result in impaired bone growth
- Debridement or incision and drainage also allow the acquisition of **deep-tissue samples** for culture

Differential diagnosis

- Osteomyelitis almost always involves **two** adjacent **vertebral** bodies and the **disc** space
- Most neoplastic processes involve a **single** vertebral body and do not extend across the disk space

Treatment, antibiotics

- Culture → broad spectrum antibiotic → narrow spectrum antibiotic:
 - *S. aureus*, cloxacillin or vancomycin
 - Streptococci: Penicillin G
 - Enteric gram-negative organisms: ciprofloxacin
 - *Serratia* spp. or *Pseudomonas aeruginosa*: piperacillin–tazobactam or imipenem
 - Anaerobes: Clindamycin or metronidazole
- A minimum of 6 weeks, with effective antibiotic

Treatment, surgery

- Not necessary with early antibiotic treatment
- May be required:
 - To remove necrotic long bone
 - In vertebral osteomyelitis:
 - To treat instability
 - To treat cord compression
 - For drainage of soft tissue abscess

Osteomyelitis
secondary to a
contiguous infection

Clinical manifestations and associated primary infections

- **Trauma:**
 - Bacteria often introduced at the time of fracture
 - Following initial corrective surgery pain improves
 - As the patient begins to bear weight pain reappears
 - Mild fever, wound erythematous, with slight discharge
 - **No other clinical or imaging procedure is fully diagnostic**
- Dental root infection leading to local bony destruction
- Deep-seated pressure sores spreading to underlying bone
- Acute purulent frontal sinusitis → osteomyelitis of frontal bone (Pott's puffy tumor)



Forehead abscess (“Pott's puffy tumor”) complicating sinusitis

Microbiology

- ***S. aureus***
- Streptococci
- Enterobacteriaceae
- *P. aeruginosa* (mostly in chronic osteomyelitis, comminuted fractures, and puncture wounds to the heel)
- Anaerobes are common in osteomyelitis
 - Of the mandible
 - Secondary to pressure
 - Caused by human and animal bites
- Polymicrobial, gram-negatives and anaerobes: sacral

Diabetic foot infections

Clinical manifestations

- Osteomyelitis secondary to **neuropathy** and **vascular** insufficiency in patients with diabetes or vascular impairment
- Almost exclusively on the lower extremities
- Starts insidiously in a patient with intermittent claudication
- Sometimes there is no pain because of neuropathy
- Ulcer in a previously traumatized skin area
- infection burrows its way to the underlying bone: toe, metatarsal head or tarsal bone



Diabetic foot



Diabetic foot

Physical examination

- Exam may elicits excruciating pain (if bone destruction has been acute)
- Cellulitis may be present: *S. aureus* or **β-hemolytic streptococcus**
- Crepitus occasionally: **anaerobes** or **Enterobacteriaceae**
- Physical examination must include:
 - Evaluation of vascular supply
 - Evaluation of peripheral nervous system

Causes and diagnosis

- The **whole gamut of pathogenic bacteria** can be responsible
- Suggest osteomyelitis:
 - Ulcer > 2 cm in diameter
 - Ability to reach bone by gently advancing a sterile surgical probe
 - Erythrocyte sedimentations rate > 70 mm in the 1st hour
 - Abnormal plain X-ray
- If probing does not detect bone and plain X-ray is normal, treatment of soft tissue infection is adequate
- **MRI** identify infection early, and avoid delays in treatment

Prognosis and treatment

- Prognosis poor due to:
 - Impaired ability of the host to eradicate infection
 - Inability of antibiotics to gain entry into the site of infection
- Treatment:
 - Antimicrobial therapy, prolonged courses, maximal doses commonly needed; **fluoroquinolones** good bone penetration
 - **Revascularization** often proves useful
 - Debridement surgery, resection or amputation may be needed
 - Hyperbaric oxygen is not useful

Assessment of clinical response

- Difficult
- Radiologic and MRI changes of osteomyelitis can worsen for several weeks despite appropriate antibiotic
- **Clinical** response and **acute phase reactants** are probably the most helpful objective criteria available for monitoring response to therapy in osteomyelitis

Prosthetic joint infections

Pathogenesis and microbiology

- Following total replacement of the hip joint
- **Acute** contiguous infections:
 - < 6 months after surgery, often within the first few days or weeks
 - From infected skin, subcutaneous tissue, or operative hematoma
- **Chronic** contiguous infections:
 - 6-24 months after surgery; usually persistent pain
 - From contamination at surgery, microorganisms of low pathogenicity
- **Hematogenous** infections:
 - > 2 years after surgery
 - From late transient bacteremia
- Coagulase-positive and coagulase-negative **staphylococci** → $\frac{3}{4}$ cases

Clinical manifestations and diagnosis

- Most patients have **no fever**
- Painful joint
- Loosening of the prosthesis, by physical examination or X-ray
- Gram stain and culture of **deep** specimen needed to distinguish:
 - **Infection** from **noninfectious** cause of loosening
 - **Infection** from **contamination**
- If intraoperative cultures, 3 to 5 should be obtained
- Cultures of samples obtained by **sonication** of prostheses



Loosening of hip prosthesis

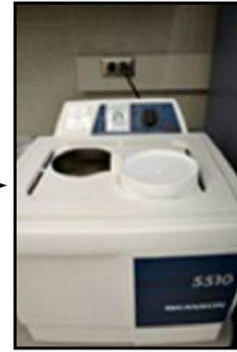
400ml Ringer's solution added



Prosthesis collection in rigid sterile container

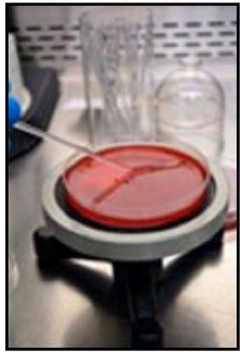


Vortex 30 seconds



Sonicate 5 minutes

Sonication of prostheses



Inoculate sonicate fluid on solid agar



Aspirate sonicate fluid



Centrifuge 5 minutes



Vortex 30 seconds

Treatment - I

- In early infection, localized debridement and systemic antibiotics may be attempted; relapses common
- All other cases:
 - **One-stage** exchange arthroplasty, excision of all components and debridement, and new prosthesis immediately put into place, sometimes with cement containing antimicrobials
 - **Two-stage** exchange arthroplasty, surgical removal of all foreign bodies and debridement, then 6 or more weeks * of antimicrobials, and reconstruction with a new prosthesis

* Longer with the more aggressive bacteria

Treatment - II

- Antibiotics:
 - **Rifampin** (penetrates the biofilm) +
 - Ciprofloxacin, levofloxacin, doxycycline, trimethoprim-sulfamethoxazole, first-generation cephalosporin, or cloxacillin
 - Take into account culture and sensitivities
 - *S. aureus*, more prolonged regimes

Septic arthritis

Pathogenesis

- Serious condition with potential for significant morbidity and disability
- Primarily hematogenous seeding of **synovial membrane** lining the joint → synovial fluid → joint swelling and erythema
- Acute inflammatory reaction with polymorphonuclears
- Cytokines and **proteases** are released into the synovial fluid
- If not quickly treated, cartilage damage and eventually narrowing of the joint space

Pathogenesis and predisposing factors

- Causes of bacteremia leading to septic arthritis:
 - Urinary tract infection
 - Intravenous drug abuse: sternoclavicular joints
 - Intravenous catheters
 - Soft tissue infections
 - Bacterial endocarditis, particularly by *S. aureus* or *Enterococcus* spp.
- Predisposing conditions:
 - **Underlying joint disease**, as rheumatoid arthritis and osteoarthritis
 - New immunosuppressive agents to control rheumatoid arthritis
 - Minor trauma
 - Intra-articular injection of corticosteroids



Sternoclavicular joint arthritis

Microbiology

- *S. aureus* the most common
- **Gram-negative rods**, elderly, often secondary to urinary tract infection
- *Neisseria gonorrhoeae*, young adults, sometimes as disseminated gonococcal infection
- *Listeria monocytogenes* or *Salmonella* spp., patients taking tumor necrosis factor inhibitors
- Parvovirus B19, hepatitis B virus, and other virus, bilateral
- *Mycobacterium* spp. and fungi, after intra-articular corticosteroids
- *Borrelia burgdorferi*, Lyme arthritis

Clinical manifestations

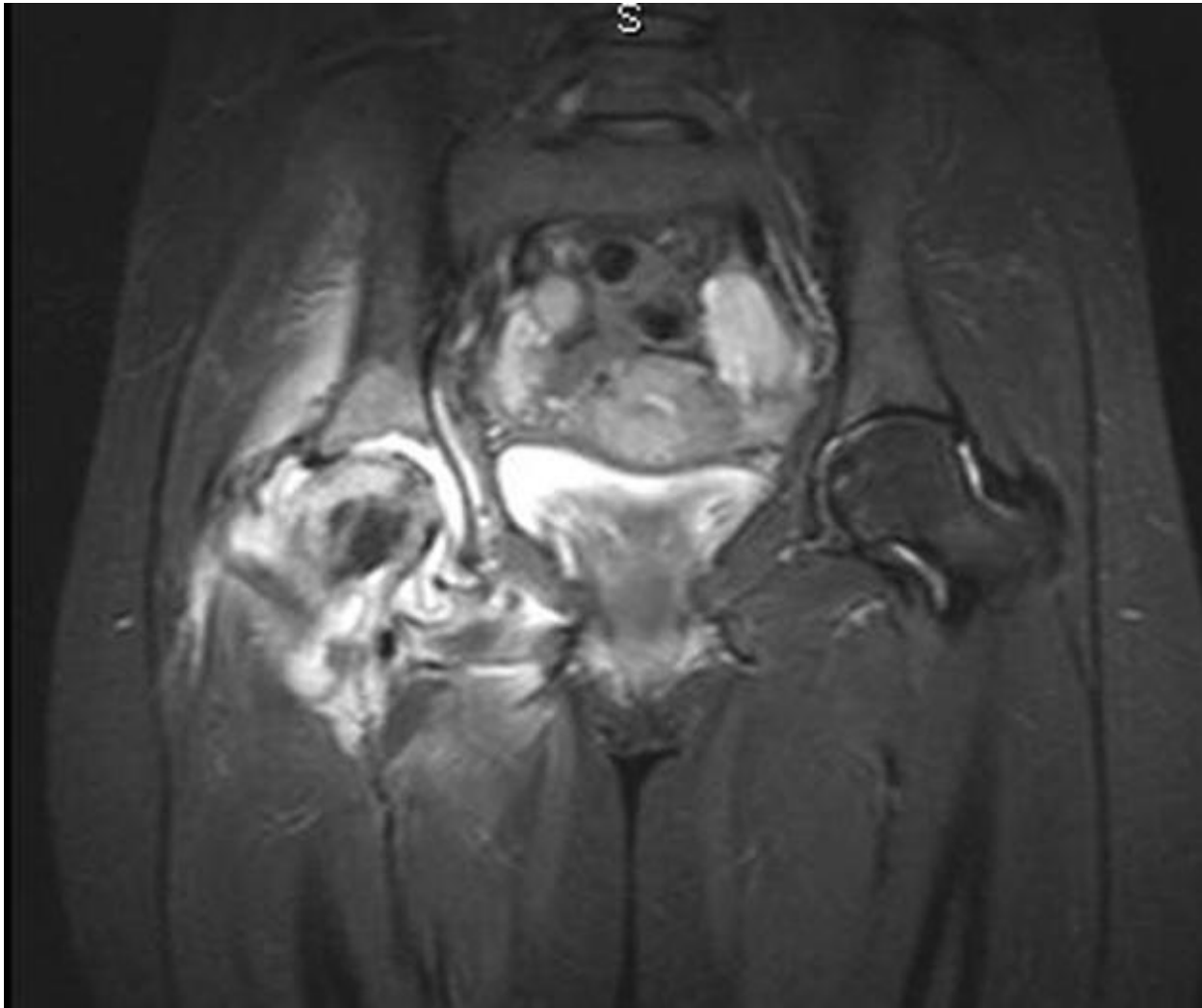
- **Swelling and pain in a single joint accompanied by fever**
- Elderly patients may be afebrile at the time of presentation
- Joint is warm, and movement provokes **exquisite** pain
- Connective tissue diseases, bilateral arthritis
- The most commonly involved joints:
 - In adults: knee (40-50 %) and hip (15-20%)
 - In children: hip (60%) and knee (35%)
- Any patient with monoarticular arthritis should be considered to have septic arthritis until proven otherwise



Septic arthritis of the knee



Septic arthritis of the left hip



Acute right hip arthritis

Diagnosis: analysis of synovial fluid

- Leukocyte count:
 - $> 200/\text{mm}^3$ = inflammatory
 - Acute infection often $> 50,000/\text{mm}^3$, polymorphonuclears predominate
- Gram and culture
- Blood cultures positive in 50 % of cases
- Culture in selective media if *N. gonorrhoeae* suspected
- PCR for *B. burgdorferi* or *N. gonorrhoeae*
- Crystals: infections and crystal arthropathy coexist

Treatment

- Drainage and washing of the purulent exudate by arthroscopy or by surgery, in particular for *S. aureus* or gram-negative infection
- Antibiotic based on gram stain, culture results, or clinical presentation, for 3–4 weeks:
 - *N. gonorrhoeae*, gram negative rods: ceftriaxone
 - *S. aureus*: cloxacillin or vancomycin

Outcome

- Adverse in general, particularly in:
 - The elderly
 - Patients with preexisting joint disease
 - Infection in a joint containing synthetic material
- 1/3 of patients experience significant residual joint damage

Disseminated gonococcal infection

Pathogenesis and predisposing factors

- In 1-3 % of patients infected with *N. gonorrhoeae* urethritis
- Predisposing factors:
 - **Delay in antibiotic treatment**
 - Congenital or acquired deficiencies of complement C5–C8
 - Bacterial virulence factors:
 - Porin serotype IA (bacterium more serum resistant)
 - Opa proteins that favor the formation of transparent colonies on culture
- In most cases **after asymptomatic urethritis**
- Women > men
- Often follows **menstruation** or delivery
- Most strains causing disseminated disease are penicillin sensitive

Clinical manifestations

- Primarily a disease of sexually active young adults or teenagers
- Tenosynovitis, dermatitis, and **polyarthriti**s syndrome:
 - First: fever, malaise, and arthralgias
 - Then: inflammation of tendons in **wrists, fingers**, ankles and toes
 - Tenderness over the tendon sheaths, pain exacerbated by movement
 - Pustular, pustular-vesicular, hemorrhagic or papular skin lesions; often periarticular, usually 4-10, resolving over 3-4 days
 - If untreated, may progress to purulent arthritis
- Purulent arthritis without skin lesions: similar to other of septic arthritis



Gonococcal arthritis



Disseminated gonococcal infection



Disseminated gonococcal infection

Diagnosis

- Blood culture, positive in about one half of cases, especially in patients with the tenosynovitis–dermatitis–polyarthritiis syndrome
- Gram and culture of joint aspirate
- Gram and culture of cervical and urethral exudates and of skin lesion scrapings
- PCR of urine for gonococcus

Treatment

- Ceftriaxone 1 g daily, continued for 24-48 hours after clinical improvement, then switched to oral cefixime, ciprofloxacin, or levofloxacin to complete 14 days
- Alternative regimens: other third-generation cephalosporins or spectinomycin
- Drainage
- Seldom results in residual joint damage

Key messages

To remember...

Bone and joint infections represent a broad range of acute and chronic diseases, frequently associated with incapacitating complications

Further reading

Used references

- Southwick F. Infectious disease. A clinical short course. 3rd Edition. New York: McGraw-Hill, 2014. Chapter 11.
- Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J, editors. Harrison's principles of internal medicine. 18th ed. New York: McGraw-Hill, 2012. Chapter 126, 144 and 334.
- Romanò CL, Romanò D, Logoluso N, Drago L. Bone and joint infections in adults: a comprehensive classification proposal. Eur Orthop Traumatol 2011; 1: 207-17.

Preparing the exam

- Southwick F. Infectious disease. A clinical short course. 3rd Edition. New York: McGraw-Hill, 2014. Chapter 11.
- These slides.