MED437
KING SAUD UNIVERSITY

MICROBIOLOGY
437

Microbiology - Bone and joint infections

Team 437

Red : Important
Black: Doctors slides
Grey : Extra Info
Green: Notes

Please check our editing file frequently.

Msk editing file

Objectives

- Define osteomyelitis and arthritis
- Know that the two conditions can happen together or separately
- Differentiate between acute and chronic osteomyelitis and arthritis
- Know the pathogenesis and risk factors of both osteomyelitis and arthritis
- Realize that bone and joint infections can be acquired through blood or directly from adjacent affected organs and tissues.
- Know the commonest causative agents of arthritis and osteomyelitis.
- Know the laboratory diagnosis and investigation of both conditions.
- know the management and treatment of both osteomyelitis and arthritis.

Introduction

Contiguous: Spreads via surrounding infected tissues. (Usually after surgeries, fractures and car accidents.)

Blood-borne: Spread through contamination by blood. (Usually with systemic infections.)

1. Bone & joint infections may exist separately or together.
2. Both are more common in infants and children.
3. Usually caused by blood borne spread ,but can result from local trauma or spread from contiguous soft tissue infection.
4. Often associated with foreign body at the primary wound site.
5. If not treated leads to devastating effect.

Adults are more prone to undergo surgeries more often than children, while children are usually more active and so are more prone to trauma. That explains the different ways of how the infection gets introduced in comparison to the patient's history. (Age, accidents, recent surgeries... etc.)

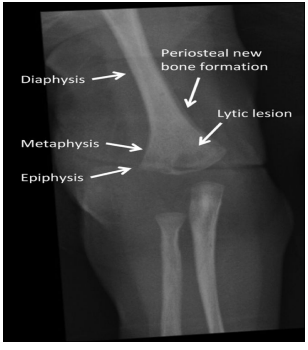
1. If not treated leads to devastating effect.

Because the accumulation of pus destroys blood vessels. Infection causes inflammation and resultant tissue necrosis producing serious damage. If this developed, cartilage or bone becomes totally separated from blood flow, and then, no healing process will occur.

Osteomyelitis overview

Radiography of acute osteomyelitis

Acute Osteomyelitis



- Definition: An acute infectious process of the bone and bone marrow.
- How the pathogen reaches the bone:

1. **Hematogenous route** (blood)
2. **Contiguous soft tissue focus** (postoperative infection, contaminated open fracture, soft tissue infection , puncture wounds)
3. **In association with peripheral vascular disease "chronic diseases"** (diabetes mellitus ,severe atherosclerosis, vasculitis)

- Duration:

  - **short duration** (few days for hematogenously acquired infection).
  - **last several weeks to months** (if secondary to contiguous focus of infection).

Etiology, Epidemiology & Risk Factors

Infants: S.aureus, group B streptococci, E.coli.

Children: S.aureus, group A streptococci, H.influenzae.

Site : Metaphysis of long bones (femur,tibia & humerus)

- Primary hematogenous is most common in infants & children.
- Adults: Hematogenous cases less common, but may occur due to reactivation of a quiescent(state of inactivity) because of infection from infancy or childhood.
- Most cases are due to S.aureus.

Septic arthritis is *common* as the infection begins in the *Diaphysis*.

Team 436

How they reach	Risk Group	
Primary Hematogenous route site:(Metaphysis of long bones)	Children and infants common Adult less common (may occur due to reactivation of a quiescent (خامد) focus of infection from infancy or childhood)** -most cases are due to S.AUREUS -S. Aureus septic arthritis (begins in the diaphysis) -Vertebral- GU infection -Candida –Venous Catheter	**Infant :** S.aureus, group B streptococci , gram –ve rods like E.coli. **Children:** S.aureus, group A streptococci, H.influenzae.
Contiguous soft tissue focus	**Post operative** infection, **contaminated** open fracture, soft tissue infection , puncture wounds	Gram positive cocci, Gram negative bacilli, anaerobes, and poly-microbial infection.
Special clinical situations	**Prosthesis (أعضاء صناعية)**	**Coagulas -negative staphylococci, and corynebacterium** (normal flora of skin) Propionebacterium, and S.aureus in foreign body infections
	Nosocomial infections (hospital acquired infection) and IV drug use	Enterobacteriacea and Pseudomonas
	Fist injuries, and diabetic foot and dicubitus ulcers,	Streptococci ,, anaerobes
	in sickle cell patients	a.Aureus , Salmonella or S. **pneumoniae**
	Human/ animal bites;	Eikenella, Pasturella multocida
	AIDS. Mostly chronic	M.tuberculosis or M. avium (Mycobacterium tuberculosis (MTB) or Mycobacterium avium)
	Infection after trauma, injury or surgery	S.aureus, group A Streptococcus, Gram negative rods, anaerobes.

-RED: very important, Make sure you know it all.- The rest: give it a quick read and focus on the underlined.

**معناه شخص أصيب بانفكشن وهو صغير ورجعت له لمن كبر

Clinical presentation & investigation findings

- Acute osteomyelitis usually of abrupt "sudden" onset
- Systemic manifestations occurs in less than 50% of patients
- Acute onset of bone pain, fever with rigors and diaphoresisغزير تعرق.
- Symptoms usually of less than 3 week's duration

Clinically

- fever
- localized pain
- heat
- swelling
- tenderness of affected site (one or more bones or joints affected in hematogenous spread)
- May be local tissue infection (abscess or wound) .

Blood findings

-leukocytosis

-High ESR

-High C-reactive protein.

X-ray findings

Early stages: normal

Later stages: Swelling of soft tissues followed by elevation of periosteum ,demineralization and calcification of bone.

Differential diagnosis (different diseases)

- ★ Primary and metastatic bone malignancies
- ★ Trauma
- ★ Acute rheumatic arthritis
- ★ Hemarthrosis
- ★ Ewing sarcoma
- ★ Vertebral compression fracture.

Diagnosis of acute osteomyelitis

Blood culture:
Bacteremia "presence of bacteria in blood" common

If blood culture is negative:
biopsy of periosteum or bone,
or needle aspiration of overlying abscess

Blood test:
complete blood and differential counts

Erythrocyte sedimentation rate (ESR): elevated but could be normal

C-reactive protein

Imaging studies:
X-RAY, MRI,
CT-SCAN

Management & Treatment

MSSA (methicillin sensitive S.aureus):
Cloxacillin, or Clindamycin .

MRSA(methicillin resistant S.aureus):
Vancomycin , Clindamycin, Linezolid, or TMP-SMX.

Polymicrobial infection:
Piperacillin-Tazobactam or Quinolone with Metronidazole.

-

Duration: several weeks to ensure cure and prevent progression to chronic osteomyelitis.

-

Surgical drainage: (as needed) if there is local purulent process.

Management and treatment from team 436 (Parts in red are most important, the doctor highlighted in the lecture

Organisms	Antibiotics	Duration/Surgery/complication and follow up
Methicillin sensitive (MSSA) Ex: *Staph.aureus*	Cloxacillin, cefazolin or Clindamycin .	• Early treatment is critical • Treat for 2-4 weeks parenteral (I.V) followed by oral therapy for a total of at least 6 weeks. • Surgery for neurological complications, para-vertebral abscess & hip joint involvement. • Complications: septicemia, metastatic abscesses, septic arthritis, chronic osteomyelitis, loss of limb ,or paravertebra abscess. • Monthly ESR for 3 months and at 6 months useful to document treatment. • Cases due to contiguous source more difficult to eradicate, Relapse common (50%) , surgery indicated.
Methicillin resistant(MRSA) Ex: *Staph.aureus*	**Vancomycin followed by Clindamycin**, Linezolid, or TMP-SMX (cannot use Beta-Lactam antibiotics)	
Polymicrobial* infection:	Ampicillin-Sulbactam, Piperacillin-Tazobactam or Quinolone with Metronidazole.	
S.epidermidis:	Vancomycin and Rifampicin	
Enterobacteriacae:	Ceftriaxone	
Other Gram negative bacilli:	Quinolones	
P. aeruginosa:	Cefepime, Meropenem, or Piperacillin +/- Aminoglycoside.	
Anaerobes:	Metronidazole or Clindamycin	

Chronic Osteomyelitis

General Risk Factors:	Host Risk Factors
1. Penetrating trauma 2. Prosthetic devices 3. Animal bites 4. IV drug use	1. Peripheral vascular disease 2. Peripheral neuropathy 3. Sickle cell disease 4. Diabetes mellitus 5.Immunocompromised states

What is it? A chronic infection of the bone and bone marrow usually secondary to inadequately treated or relapse of acute osteomyelitis.

Management difficult , prognosis poor. Prognosis: the end result

Infection may not completely cured.

May recur many years or decades after initial episode.

Most infections are secondary to a contiguous focus or peripheral vascular disease.

Chronic infection due to hematological spread is rare.

TB and Fungal are common causes (if patient is taking too long to heal then think of TB especially in elderly and immunocompromised patients)

Acute is caused mostly from blood

Chronic from peptic vascular disease.

Chronic Osteomyelitis

Polymicrobial (more than one organism) infection common with decubitus ulcers and diabetic foot infections

TB and fungal osteomyelitis clinically have indolent (lazy\idle) "chronic" course

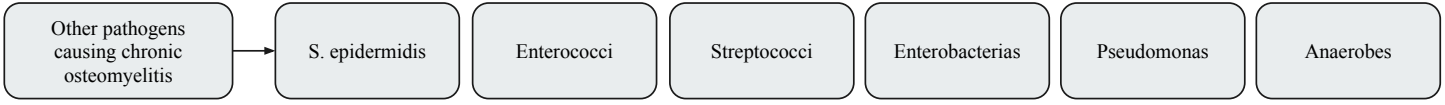
Most common pathogen: S. Aureus

Mycobacteria and fungi (ex: candida and aspergillus) may be the cause in immunosuppressed patients.

MTB osteomyelitis primarily results from haematogenous spread from lung foci or as an extension from a caseating lymph bone (50% in spine). It resembles Brucella osteomyelitis.

TB & Brucella are common in KSA. may come as saq case.

Haematogenous osteomyelitis due to fungi eg. Candida species, Aspergillus species and other fungi may occur



All are endogenous.

Patient presentation and Differential Diagnosis

Patient Presentation

- Acute symptoms and systemic manifestations are uncommon.
- Sinus tract
- Persistent wound drainage
- Chronic non-healing ulcer
- Local signs may be absent except during acute exacerbation.
- Overlying skin may be scarred and adherent to the involved bone.

Differential Diagnosis

- Osteoid osteoma
- Osteosarcoma
- Secondary bony metastases
- Paget's disease of the bone
- Gout

Diagnosis of chronic osteomyelitis

Radiological

- Radiologic changes complicated by the presence of bony abnormalities
- MRI helpful for diagnosis and evaluation of extent of disease.
- **Combined** bone scan and Indium WBC scan.

Laboratory

- WBC normal, ESR elevated but not specific.
- Blood culture not very helpful- because as bacteremia rare.
- **Definite microbiological diagnosis** by culture of bone biopsy or FNA & Histological examination
- Surgery for diagnosis and therapeutic purposes
- Wound /sinus culture not reliable. Isolation of MRSA or vancomycin resistant enterococci should initiate infection control measures.

Blood culture bottles

Management and Treatment

Extensive surgical debridement with antibiotic therapy.
Parenteral antibiotics for 3-6 days weeks followed by long term oral suppressive therapy.
Some patient may require life long antibiotic, others for acute exacerbations.

MSSA: Cloxacillin

MRSA & S.epidermidis: Vancomycin then oral clindamycin or TMP-SMX.

MTB: -4 drugs-:
1-INH, 2-RIF, 3-Pyrazinamide, 4-Ethambutol for 2 months, followed by RIF + INH for additional 4 months.

Total=6month
بعض المرضى يحتاجون سنة أو ٩ شهور

Brucella: is treated with Tetracycline and Rifampicin for 2 to 3 months.

Other bacteria: treat as acute osteomyelitis.

Complications & Prognosis

Complications

- Recurrence
- Loss of limb
- Pathological fractures
- Primary epidermoid carcinoma of sinus tract
- Malignant histocytoma
- Secondary amyloidosis
- Lymphoma & multiple myeloma(rare)

Prognosis

- Relapses are Frequent

Septic Arthritis

Septic(infectious)Arthritis: is inflammation of the joint space secondary to infection.

Generally affects a single joint and result in suppurative inflammation.

Maybe caused by bacteria(Most common and acute) or viruses.

Haematogenous of joint is most common.

Common symptoms:
1- pain.
2- swelling.
3- limitation of movement.

Diagnosis by Arthrocentesis to obtain synovial fluid —>For analysis: Gram culture & sensitivity.

Drainage & antimicrobial therapy important management.

يدخلون إبرة للمفصل ويسحبون synovial fluid ويعملون analysis

Common causes of septic arthritis

Staph.aureus is the most common organsim

Age/special conditions	Common organism
Neonates	1. S.aureus 2. Group B Streptococcus 3. Gram negative rods (eg. E.coli, Klebsiella, Proteus, Pseudomonas) .
Infants/ children	1- Staph.aureus 2- Group A Streptococcus 3- Strept.pneumoniae 4- Hemophilia. influenzae type b
Adults	1- S.aureus 2- Neisseria gonorrhoeae is a pathogen not normal flora!!
Sickle cell disease	1- Salmonella species 2- S.aureus
Trauma/ surgical procedure	S.aureus
Chronic arthritis	1- MTB 2- Fungi
Prosthetic arthritis	Skin flora

-Self limiting: A disease restricted in duration by its own pattern of characteristics and not by other influences.
-Reactive arthritis means that the arthritis is from previous infections.

Other causes of Arthritis

Viruses

1. Rubella
2. Hepatitis B
3. Mumps
4. Parvovirus B19
5. Varicella
6. EBV
7. Adenovirus ..etc.

These are **self-limiting**

Reactive arthritis
Due to

- Campylobacter jejuni causes diarrhea
- Yersinia enterocolitica not common in ksa
- Some Salmonella species

Non-infectious causes

1. Rheumatoid arthritis
2. Gout
3. Traumatic arthritis
4. Degenerative arthritis

Risk factors & Pathogenesis

1- Gonococcal infection

- **Common cause** in **young, sexually active adults**.
- **Caused by Neisseria gonorrheae**.
- **Leads to disseminated infection** secondary to **urethritis/cervicitis**.
- **Initially present with polyarthralgia, tenosynovitis, fever, skin lesions**.
- **If untreated leads to suppurative monoarthritis**.

2- Nongonococcal arthritis

- **Occurs in older adults**.
- **Results from** introduction of organisms into **joint space** as a **results of bacteremia** or **fungaemia** from infection at other body sites.
- Occasionally results from **direct trauma, procedures (arthroscopy)** or from **contiguous soft tissue infection**.
- **S.aureus** is **most common cause**.
- **Other organisms** : **Streptococci** and **Aerobic Gram negative bacilli**.

3- Lyme disease

Due to **tick bite** in endemic areas (uncommon in KSA) may come as saq case

4- In Sickle Cell disease

Arthritis may be caused by **Salmonella species**.

5- Chronic arthritis

May be due to **MTB** or **Fungi**.

Gonococcal infection never happens in old people.

May come as a case:

Lyme disease is common in Scandinavia

A patient will present with skin rash and arthritis due to a tick bite.

Risk factors for long term adverse *sequelae* include: Age, prior rheumatoid arthritis, polyarticular joint involvement, hip or shoulder involvement, virulent pathogens and delayed initiation or response to therapy

Diagnosis of Septic Arthritis

1-History/examination to exclude systemic illness.

Note: history of tick exposure in endemic areas

2-Culture of joint fluid and skin lesions .

3-Blood cultures indicated

4-Arthrocentesis should be done as soon as possible:

1-Synovial fluid is cloudy and purulent.
2- Leukocyte count generally > 25,000/mm3,with predominant neutrophils.
3- Gram stain and culture are positive in >90% of cases.
4-Exclude crystal deposition arthritis or noninfectious inflammatory arthritis.

5- If Gonococcal infection suspected:

- take specimen for culture from cervix, urethra, rectum & pharynx
- DNA testing for N.gonorrheae.
- Investigate for other sexually transmitted diseases.

Treatment & Management,

Arthrocentesis with drainage of infected synovial fluid.

Repeated therapeutic Arthrocentesis often needed.

Occasionally, arthroscopic or surgical drainage/debridement

Prognosis and complications:

- Gonococcal arthritis has an excellent outcome
- Non-Gonococcal arthritis: can result in scarring with limitation of movement, ambulation is affected in 50% of cases.

Risk factors for long –term adverse sequelae include:

- ❑ Age
- ❑ Prior rheumatoid arthritis
- ❑ Poly-articular joint involvement
- ❑ Hip or shoulder involvement
- ❑ Virulent pathogens
- ❑ Delayed initiation or response to therapy

Treatment and management of nongonococcal infectious arthritis

1. MSSA: Cloxacillin or Cefazolin (it covers everything)
2. MRSA: Vancomycin
3. Streptococci: Penicillin or Ceftriaxone or Cefazolin
4. Enterobacetriacae: Ceftriaxone or Fluroquinolone
5. Pseudomonas: Piperacillin and Aminoglycoside
6. Animal bite : Ampicillin-Sulbactam

lyme disease arthritis: Doxycycline for one month.

★ Change the antibiotics according to sensitivity, Arthrocentesis can repeated and Surgery rarely required

Antimicrobial therapy should be directed at the suspected organism and susceptibility results:

1. Gonococcal arthritis: IV Ceftriaxone (or Ciprofloxacin or Ofloxacin) then switch to oral Quinolone or Cefixime for 7-10 days.

Infections of Joint Prosthesis

- Occur in 1 - 5 % of total joint replacement.
- Most infections occur within 5 years of joint replacement.
- Often caused by skin flora.
- Diagnostic aspiration of joint fluid necessary .
- Result in significant morbidity and health care costs.
- Successful outcomes results from multidisciplinary approach.

Risk factors: history of superficial wound infection, post surgical complications, underlying illness, any source of bacteremia.

Diagnosis of Prosthetic Arthritis:

A. exploration to obtain specimen for culture , sensitivity testing & histopathology.
B. Skin flora regarded as pathogens if isolated from multiple deep tissue cultures.
C. Plain X-ray may not be helpful.
D. Arthrography may help define sinus tracts.
E. Bone scan-not specific for infection.
F. ESR and C-reactive protein(CRP) may be high

Differential Diagnosis

- Aseptic loosening or dislocation of prosthetic joint
- Prosthetic debris induced cynovitis &
- hemarthrosis

Infections of Joint Prosthesis:

- **Etiology:**
  - ✓ Results from **contamination during surgery** or post op. wound infection adjacent to the prosthesis.
  - ✓ Factors delay healing (hematoma, ischemia)
  - ✓ Occasionally result from **bacteremia**
  - ✓ Prosthesis & bone cement predispose to infection
  - ✓ Occurs at the prosthesis-bone interface
  - ✓ Bacteria adhere to biomaterials and develop a biofilm that protect them from host defenses and antimicrobial agents.
  - ✓ **Mostly caused by coagulase negative staph., or *S.aureus*.**
  - ✓ Occasional pathogens: **streptococci, enterococci ,and anaerobes**
  - ✓ Usually **single pathogen** ,occasionally **polymicrobial**
- **Patient Presentation:**
  - ✓ Subacute onset
  - ✓ *S.aureus*, streptococci,Gram negative rods can cause acute ,rapidly progressive infection
  - ✓ **Joint pain** ,**swelling** most common
  - ✓ Fever with acute ,early postsurgical infections
  - ✓ Cellulitis, cutaneous wound, or discharging sinus overlying the joint.

Management & Treatment:

- Surgical debridement and prolonged antimicrobial therapy
- Surgery: removal of prosthesis
- Antibiotic –impregnated cement during reimplantation
- Antimicrobial for 6 weeks: Begin empiric IV antibiotic to cover MRSA and Gram negative rods (Vancomycin+ Cefepime, Ciprofloxacin, or Aminoglycoside)
- Chronic therapy with oral drug if removal of prosthesis not possible.

Quiz

1. Which of the following is the cause of septic arthritis for children :

a.Group A streptococcus b.Group B streptococcus c.Neisseria gonorrhoeae

2.The most common cause of osteomyelitis is:

a.Staphylococcus Aureus b.Streptococcus c.Salmonella

3.Gonococcal infection is common for :

a.Old adults b.Young sexually active adults

4.Gonococcal has what type of outcome?

A.excellent b.bad c.needs lifelong treatment to live

1.A 2.A 3.B 4.A

SAQ

A man presents with persistent wound drainage, skin scarring overlying affected bone, and non-healing ulcers.After taking history we find he has camels that he often drinks their milk.

What is the disease? Chronic osteomyelitis

What caused it? Brucella from the unpasteurized milk.

Treatment? Tetracycline and Rifampicin for 2 to 3 months.

A man from scandinavia presents with tick bites and pain , swelling of his joints along with limitations of movement.

What is his disease? Septic arthritis

How is diagnosed? Arthrocentesis, synovial fluid should be cloudy and purulent.

How should we treat it? Repeated therapeutic Arthrocentesis often needed.Occasionally, arthroscopic or surgical drainage/debridement.

Team members:

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Some videos for understanding the lecture:

bone infection

Overview of this lecture