Musculoskeletal System

Sakchai Chitpakdee, M.D.

Contents
- Bones
  - Osteoporosis
  - Rickets, osteomalacia, hyperparathyroidism, renal osteodystrophy
  - Fracture
  - Osteonecrosis (Avascular necrosis)
  - Infections
  - Bone tumors and tumor-like lesions

- Joints
  - Arthritis and osteoarthritis
  - Tumor and tumor-like lesions of joints

- Skeletal muscle
  - Muscular dystrophies
  - Inflammatory myopathies
  - Myasthenia Gravis

Osteoporosis
- Increased porosity of skeleton resulting from reduced bone mass
  - Localized: disused osteoporosis
  - Generalized: metabolic bone disease
    - Primary: Senile, postmenopausal, idiopathic
    - Secondary: Vit D deficiency, Steroids
  - Most common:
    - Senile osteoporosis
    - postmenopausal osteoporosis

Osteoporosis
- Clinical course:
  - Vertebral fractures: thoracic and lumbar regions, painful
  - Multiple fractures → loss of height, lumbar lordosis and kyphoscoliosis
- Diagnosis:
  - 30-40% bone loss → detected by radiographs
  - Dual-energy absorption and quantitative CT
  - Biopsy

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Osteoporosis

- Prevention and treatment:
  - Exercise
  - Calcium and vitamin D intake
  - Estrogen replacement
  - Biphosphonate
  - Recombinant PTH

Rickets and Osteomalacia

- Defect in matrix mineralization
- Lack of vitamin D or disturbance of its metabolism
- Children → “rickets”
  - Skeletal deformities
- Adults → “osteomalacia”
  - Osteopenia → fracture

Hyperparathyroidism

- PTH → ↑ osteoclastic activity
- Osteitis fibrosa cystica (brown tumor)
- Clinical features:
  - Fracture, bone deformities
  - Joint pain and dysfunction

Renal Osteodystrophy

- Skeletal changes of chronic renal disease:
  - High turnover osteodystrophy
    - Osteoclastic bone resorption (osteoporosis)
  - Low turnover or aplastic disease
    - Matrix mineralization (osteomalacia)
- Pathogenesis:
  - Vitamin D def. → hypocalcemia → PTH ↑
  - Hyperphosphatemia → PTH ↑
  - Metabolic acidosis → bone resorption ↑
  - Aluminum deposit → bone mineralization ↓
Fractures

- Classification:
  - Complete vs. incomplete
  - Closed (simple) vs. Opened (compound)
  - Comminuted (splintered)
  - Displaced
  - Pathologic fracture (underlying bone dis.)
  - Stress fracture (repetitive loads)

Reparative process:

- 1st week → organizing hematoma (soft tissue callus, procallus)
- 2nd or 3rd week → bony callus (cartilage and bone formation)

Delayed healing: → nonunion

- Displaced, comminuted, compound fractures
- Inadequate immobilization
- Infections
- Calcium ↓, phosphorus ↓, Vitamin def. diabetics, vascular insufficiency

Osteonecrosis (AVN)

- Ischemia → infarction

- Mechanisms:
  - Vascular interruption (fracture)
  - Corticosteroids
  - Thrombosis and embolism (nitrogen bubbles, dysbarism)
  - Vessel injury (vasculitis, radiation)
  - ↑ Intraosseous pressure and vascular compression
  - Venous hypertension

Clinical course:

- Subchondral infarcts → chronic pain, 2nd osteoarthritis
- Medullary infarcts → clinically silent, painful, collapse

- Pyogenic osteomyelitis

  - Bacterial infections:
    - S. aureus (80-90%) E. coli, Pseudomonas, Klebsiella: IVDU, GU tract
    - Mixed organisms: fracture, direct spread
    - H. influenzae: neonatal period
    - Salmonella: sickle cell anemia
  
  - Spread: hematogenous, extension from contiguous sites, direct implantation
Infections—Osteomyelitis

- **Pyogenic osteomyelitis**
  - **Sites:**
    - Neonate: Metaphysis, epiphysis
    - Children: Metaphysis
    - Adult: Epiphysis, subchondral
  - **Clinical course:**
    - Acute systemic illness, fever, malaise, leukocytosis, throbbing pain
    - X-ray: lytic bone destruction
    - Treatment: antibiotics and surgical drainage
  - 5-25% → chronic osteomyelitis

- **Tuberculous osteomyelitis**
  - 1-3% of patients with pulmonary or extrapulmonary TB have osseous infection
  - Hematogenous spread from visceral organs or direct extension
  - Spine infection (Pott disease): thoracic and lumbar vertebrae
  - More destructive and resistance to therapy than pyogenic osteomyelitis

Bone tumors and Tumor-like lesions

- **Hematopoietic (40%)**
- **Chondrogenic (22%)**
- **Osteogenic (19%)**
- **Unknown origin (10%): giant cell tumor**
- **Micellaneous:**
  - Fibrous and histiocytic
  - Vascular
  - Lipogenic
  - Neurogenic

Bone tumors and Tumor-like lesions

- **Characteristic:**
  - **Osteosarcoma:**
    - Adolescence, metaphysis around the knees
  - **Chondrosarcoma**
    - Adulthood, trunk, limb girdle, proximal long bones
  - **Giant cell tumors and chondroblastoma:**
    - Epiphysis of long bones
  - **Ewing sarcoma, osteofibrous dysplasia, adamantinoma**
    - Diaphysis

Bone-forming tumor

- **Osteosarcoma:**
  - Most common primary bone tumor
  - Age: 75% (children, <20 yo) 25% (elderly)
  - Secondary osteosarcoma: Paget disease, bone infarct, irradiation
  - Sites: metaphyseal region of long bone
  - Clinical: painful enlarging mass
  - X-ray: destructive, lytic and blastic mass with permeative margin, "Codman Triangle"
  - Treatment: Chemotherapy, limb salvage
Cartilage-forming tumor

- Osteochondroma:
  - Exostosis
  - Solitary and multiple (hereditary)
  - Late adolescence and early adulthood
  - Metaphysis of long bones
  - Clinical: slow-growing mass, can be painful, rare (<1%) → chondrosarcoma

Cartilage-forming tumor

- Chondrosarcoma:
  - Second most common malignant matrix-producing tumor of bones
  - Age 40 or older
  - Malignant transformation from enchondroma, osteochondroma, chondroblastoma
  - Sites: central portions of skeleton, pelvis, shoulder, and ribs
  - Clinical: painful enlarging mass, fracture
  - X-ray: Destructive radiolucent mass
  - Treatment: Surgical excision, chemotherapy

Miscellaneous tumors

- Giant cell tumor:
  - Benign but locally aggressive tumor
  - Patients in twenties to forties
  - Sites: epiphysis and metaphysis of any bones (common: distal femur and proximal tibia)
  - X-ray: large, purely lytic, eccentric and erode into subchondral bone plate
  - Treatment: Conservative surgery
  - 40-60% recurrent, 4% metastasis to lung
Metastatic disease

- **Adults:**
  - Prostate, breast, kidney, and lung

- **Children:**
  - Neuroblastoma, Wilms tumor, osteosarcoma, Ewing sarcoma, rhabdomyosarcoma

- **X-ray:**
  - Multifocal or solitary (kidney, thyroid)
    - Lytic: Kidney, lung, GI and melanoma
    - Blastic: Prostate

Joints

- **Osteoarthritis:**
  - Degenerative joint disease
  - Progressive erosion of articular cartilage
  - Idiopathic (primary OA): aging phenomenon
  - Secondary osteoarthritis (5%): diabetics, ochronosis, hemochromatosis, obesity
  - Women: knees and hands
  - Men: hips

Osteoarthritis

- **Pathogenesis:**
  - Aging and mechanical effects
  - Genetic factors: high bone density

- **Clinical course:**
  - Primary OA: old age (>50 yr)
  - Secondary OA: younger age, underlying dis.
  - Deep achy pain, worsen with use
  - Morning stiffness, crepitus, limitation of movement
  - Nerve root compression (osteophytes)

Rheumatoid arthritis

- **Chronic systemic inflammatory disorder:**
  - skin, blood vessels, heart, lungs, muscles, joints

- **Pathogenesis:**
  - Autoimmune disease: arthritogenic antigen ➔ CD4+ helper T cells ➔ inflammatory cytokines
  - Genetic susceptibility: HLA-DR1*0401, *0404
  - Antigens: unknown
Rheumatoid arthritis

- Clinical course:
  - 50%, slow and insidious onset: malaise, fatigue, musculoskeletal pain, joint pain
  - 10% acute onset with severe symptoms
  - Site: small joints > large joints: MCP, PIP, MTP, IP, wrists, ankles, elbows, knees
  - 20%, partial or complete remission period
  - Joint destruction, deformity: swan neck, boutonniere of fingers
  - X-ray: juxta-articular osteopenia, bone erosion with narrowing of joint space

- Laboratory tests and Dx:
  - Serum rheumatoid factor (IgM to Fc portion): not specific
  - Synovial fluid analysis: inflammatory exudate
  - Clinical criteria: 4 criteria
    - Morning stiffness
    - Arthritis in three or more joints
    - Arthritis of typical hand joints
    - Symmetric arthritis
    - Rheumatoid nodules
    - Serum rheumatoid factor
    - Typical radiographic changes

- Treatment:
  - Anti-inflammatory drugs (aspirin, NSAIDs)
  - Steroids
  - Anti-TNF antibody, soluble TNF receptor

Seronegative spondyloarthropathies

- Ankylosing spondylitis
- Reactive arthritis (Reiter syndrome and enteritis associated arthritis)
- Psoriatic arthritis
- Arthritis associated with inflammatory bowel disease
Ankylosing spondyloarthritis
- Rheumatoid spondylitis and Marie-Strumpell disease
- Sites: axial, sacriiliac & apophyseal joints
- Age: 20-30 yr, M>F
- 90% HLA-B27 positive
- Clinical: low back pain, spinal immobility (ankylosis), fracture of spine, aortitis, amyloidosis

Reactive arthritis
- Noninfectious arthritis of appendicular skeleton occurs within one months of primary infection localized elsewhere
  - GU: clamydia
  - GI: shigella, salmonella, Yersinia, Campylobacter
  - Reiter syndrome: arthritis, nongonococcal urethritis/cervicitis, conjunctivitis
  - 80% HLA-B27 positive
  - Extraarticular: balanitis, carditis

Infectious arthritis
- Suppurative arthritis:
  - Bacteria: gonococcus, Staphylococcus, Streptococcus, Haemophilus influenza, E. coli, salmonella, Pseudomonas
  - Children <2 yr: H. Influenzae
  - Adults: S. aureus
  - Young women: Gonococcus
  - Sickle cell anemia: Samonella
  - Painful joint, fever, leukocytosis
  - Knees, hip, shoulder, elbow, wrist

Gout and Gouty arthritis
- Transient attacks of arthritis initiated by crystallization of monosodium urates (needle shape, neg. birefringent) within joints
- Pathogenesis: hyperuricemia → gout
  - Age: 20-30 yr after hyperuricemia
  - Genetic: Lesch-Nyhan syndrome
  - Heavy alcohol consumption
  - Obesity
  - Drugs: thiazides
  - Lead toxicity

Gout and Gouty arthritis
- Clinical course: four stages
  - Asymptomatic hyperuricemia: puberty male or menopause women
  - Acute gouty arthritis: 50% MTP joint, ankles, heels, knees, wrists, fingers, elbows
  - Intercritical gout
  - Chonic tophaceous gout: 12 years after first attack
  - Extra-articular: atherosclerosis, hypertension, renal colic, gouty nephropathy
**Pseudogout**
- Calcium pyrophosphate crystal deposit disease (CPPD)
- Age: over age 50
- Type: Idiopathic, hereditary and secondary (joint damage, hyperparathyroidism, hemochromatosis, hypomagnesemia, hypothyroidism)
- Clinical: asymptomatic, acute, subacute, chronic arthritis of knees, wrists, elbows, shoulder, ankles

**Tumor and Tumor-like lesions**
- Ganglion cysts:
  - Size: 1 to 1.5 cm near joint capsule or tendon
  - Site: wrists, fingers
  - Etiology: Cystic degeneration
- Synovial cysts:
  - Baker cyst of knees in RA patients
  - Synovial protrusion (diverticulum)

**Muscular dystrophies**
- X-linked muscular dystrophy (Duchene and Becker muscular dystrophy)
  - Pathogenesis: Dystrophin gene, Xp21
    - Deletion or frameshift mutation (DMD), Point mutation (BMD)
  - Clinical:
    - DMD normal at birth, delayed walking, clumsiness
    - Weakness begins in pelvic girdles, shoulder girdles
    - Enlargement of calf muscle (pseudohypertrophy)
    - Increased serum creatine kinase
    - Death from respiratory failure, pulmonary infection and cardiac decompensation
    - BMD: later onset and less severe
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- Immune-mediated loss of acetylcholine receptors (AChRs); autoimmune disease
- W>M, Age < 40
- Thymic hyperplasia (65%), thymoma (15%)
- Clinical: extraocular muscles (ptosis, diplopia) → generalized weakness, respiratory paralysis
- Rx: anticholinesterase agents, prednisone, plasmapheresis, resection of thymoma

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