Metabolic bone disease

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Abstract

Metabolic bone disease encompasses a diverse group of disorders associated with altered calcium and phosphorous homoeostasis. Although many of these disorders are quite common, they may be difficult to distinguish on the basis of history, physical examination and imaging studies. In clinical practice, metabolic bone disease is often silent until the patient presents with a fracture which is the ultimate complication of many metabolic bone disorders. However, other patients present with a clinical history of back pain and non-specific radiological findings of osteopenia. It is at this stage, that thorough understanding of these diverse manifestations and an accurate diagnosis is crucial to provide the best outcomes for patients with these potentially debilitating disorders. This article aims to give a thorough and succinct review of more relatively common of these diseases.

Keywords idiopathic transient osteoporosis of the hip (ITOH); metabolic bone disease; osteomalacia; osteopetrosis; osteoporosis; renal osteodystrophy; rickets

Introduction

Metabolic bone disease includes a diverse group of disorders of skeletal homeostasis. Although many of these are relatively common, they can be difficult to distinguish. A sound comprehension of the metabolic diseases that cause intrinsic biomechanical alterations and damage to the skeletal system is an essential part of orthopaedic knowledge. This article will systematically review the pertinent facts of the more relatively common of these diseases.

Conditions of bone mineral density

Osteoporosis

Osteoporosis is defined as an age-related decrease in bone mass secondary to uncoupling of osteoclast–osteoblast activity, with disruption of the bone micro-architecture.

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- World Health Organization definition
  - L2–4 lumbar vertebral density >2.5 standard deviations (T score <−2.5) below the peak bone mass of a 25-year-old sex-matched individual.
- Epidemiology:[1]
  - Incidence: 20 million people worldwide have osteoporosis
  - Male:female ratio is 1:4
  - Associated with fragility fractures
  - Wrist fractures occur most commonly at age 50–60 years
  - Vertebral fractures occur most commonly at age 60–70 years
  - Hip fractures occur most commonly at age 70–80 years
- Risk factors are listed in Table 1.
- Histology
  - Bone resorption is greater than bone formation:
    - Cancellous bone: trabeculae are thinned and decreased in number. Some are lost completely. This loss of bony struts leaves adjacent areas unsupported and therefore significantly weakened.
    - Cortical bone: decreased size of osteons and enlargement of marrow space. The cortices of long bones become thinner with age, while the overall bone diameter expands.
- Management
  - History: to include risk factors and symptoms
  - Examination
  - Blood tests:
    - Full blood count, erythrocyte sedimentation rate (ESR), biochemistry, thyroid function, bone profile
    - Prostate-specific antigen, testosterone, gonadotrophin levels (men)
    - Serum parathyroid hormone (hyperparathyroidism)
    - Plasma electrophoresis (multiple myeloma)
    - Urinary free cortisol (Cushing's disease)
    - Serum bone-specific alkaline phosphatase (osteoblast activity).
  - Plain X-ray:
    - Thinned cortices, loss of trabecular bone, kyphosis, codfish vertebra
    - >30% bone loss required to be seen on X-ray, making it an insensitive test.
  - DEXA scan (dual-energy X-ray absorptiometry):
    - Measures bone mineral density commonly in lumbar spine or hip areas and compiles scores.
- Treatment is outlined in Table 2.

Osteopetrosis (marble bone disease)

A group of bone disorders characterized by increased sclerosis and loss of the medullary canal, caused by impaired osteoclast function, leading to failure of bone resorption. This is associated with a mutation the causes a loss of function of the carbonic anhydrase II gene.

- Histology
  - Osteoclasts lack ruffled border required for effective bone resorption
  - Marrow spaces are filled with necrotic calcified cartilage
  - Empty lacunae and plugging of Haversian canals[2]

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Osteoporosis risk factors[1]

Lifestyle

- Sedentary lifestyle
- Caucasian women of European descent
- Smokers
- Low body mass index
- Low protein intake
- Heavy drinkers
- Positive family history
- Premature menopause
- Breastfeeders with low vitamin D diets

Medications

- Phenytoin therapy
- Reduces vitamin D metabolism
- Cytotoxic/antineoplastic drugs
- Selective serotonin reuptake inhibitors (SSRIs)
- Antiretroviral therapy
- Cyclosporine, furosemide
- Methotrexate
- Omeprazole
- Unfractionated heparin and low-molecular-weight heparin
- Glucocorticoids

Genetic polymorphisms

- Calcitonin receptor
- Oestrogen receptor-1
- Type 1 collagen α-1 chain (COL1A1)
- Vitamin D receptor
- Low-density lipoprotein receptor-related protein (LRP5)

Diseases

- Malabsorption syndromes
- Liver disease
- Hyperthyroidism
- Type 1 diabetes mellitus
- Cancer
- Chronic renal failure
- Chronic obstructive pulmonary disease
- Rheumatoid arthritis
- Sarcoidosis

Table 1

- Types
  - Infantile (malignant) form
    - Autosomal recessive (*TCIRG1* gene mutations cause about 50% of cases of autosomal recessive osteopetrosis)[3]
    - Most severe form
    - Clinical features: aplastic anaemia, hepatosplenomegaly
    - Radiograph: 'bone within a bone' appearance
    - Treatments:
      - bone marrow transplantation can be lifesaving
      - calcitriol ± steroids can be helpful

Treatment options for osteoporosis[2]

Bone loss ↓	Halt loss →	Bone gain ↑
• Phosphate • Bisphosphonates	• Calcium • Vitamin D • Alendronate • Calcitonin • Mild exercise (biomechanical-electrical coupling) • Pamidronate • Raloxifene • Tamoxifen	• Fluoride + • Calcium • Vitamin D • Calcitonin • Extensive exercise (biomechanical-electrical coupling)

Table 2

  - 'Tarda' (benign) form (also known as Albers-Schönberg disease)
    - Autosomal dominant
    - generalized osteosclerosis
    - Radiograph: typical 'rugger jersey' spine[4]

Paget's disease of bone (osteitis deformans)

Figure 1 shows Paget's disease of bone affecting the femur.

- Epidemiology
  - High prevalence in the UK and USA
  - Family history 15–30% cases
  - No racial difference in incidence
  - Slight male predominance
  - Increased incidence HLA-DQwl
- Aetiology
  - Likely viral (paramyxovirus) as osteoclasts contain virus-like inclusion bodies causing abnormal function.
  - Genetic predisposition: chromosome focus for familial expansile osteolysis
- Pathophysiology
  - Increased osteoclast size and number, leading to raised bone resorption
  - Following this, a compensatory increase in disorganized osteoblastic bone formation occurs

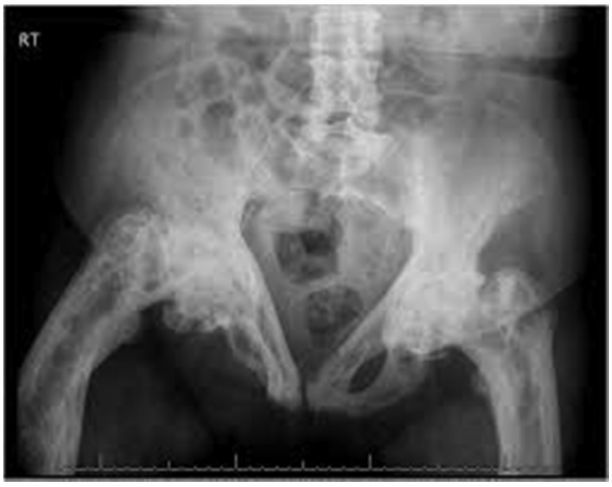

Figure 1 Paget's disease of bone affecting the femur.

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