原文題目(出處)：	Marble Bone Disease: A Review of Osteopetrosis and It Oral Health Implications for Dentists JCDA 2007;73:839-43.
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內文：

Abstract

- Osteopetrosis is one cause of osteosclerosis and may result in serious oral complications as osteomyelitis and exposed necrotic bone.
- Dentists should be aware of the disease because of its effect on osteoclast function →→ impaired wound healing.
- Purpose:
  - Review the causes, pathogenesis and differential diagnosis of osteopetrosis.
  - Provide guidance to dentists on the management of patients with osteopetrosis.

Introduction

- Marble bone disease was described in 1904 by Albers-Schonberg, a group of rare hereditary skeletal disorders, including impaired osteoclast function and have serious oral diseases.
  - A marked increase in bone density due to a defect in remodeling caused by the failure of normal osteoclast function.
  - Osteomyelitis and exposed necrotic bone may occur in osteopetrosis jaws following dental extractions. → Fatal in these fragile patients
- Estimated prevalence: 1 : 100,000~500,000
- 2 major clinical forms:
  - ✓ the autosomal dominant adult form (benign) → few/no symptoms
  - ✓ the autosomal recessive infantile form (malignant) → fatal (untreated)

Pathogenesis

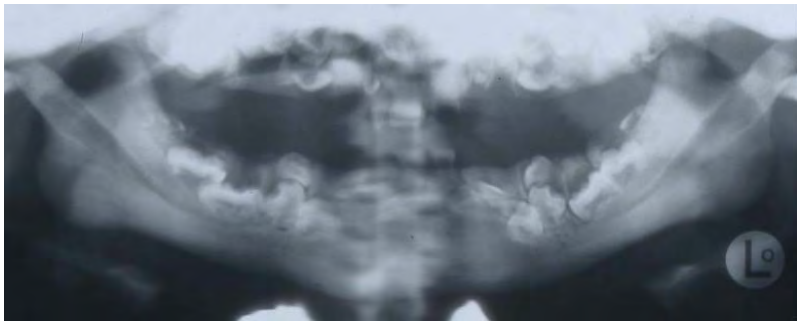
- Most forms of osteopetrosis are transmitted as autosomal traits.
- The molecular basis remains unclear.
- The gene for adult osteopetrosis has be mapped to chromosome 1p21.
- The pathogenesis of all forms of osteopetrosis involves diminished osteoclast-mediated skeletal resorption.
  - ✓ The number is often increased.
  - ✓ Fail to function → bone is not resorbed and remodeling.
- Defective osteoclastic bone resorption:
  - ✓ Continued bone formation
  - ✓ Endochondral ossification
  - ✓ Cortical bone thickening
  - ✓ Cancellous bone sclerosis
- The cause of osteoclast failure are unclear.
  - ✓ Abnormalities in the osteoclast stem cell, osteoclast precursor cells, the mature heterokaryon, or in the bone matrix.
  - ✓ the synthesis of abnormal parathyroid hormone(PTH)
  - ✓ defective production of interleikin 2(IL-2)
  - ✓ superoxide
- Impaired bone resorption results in skeletal fragility because fewer collagen

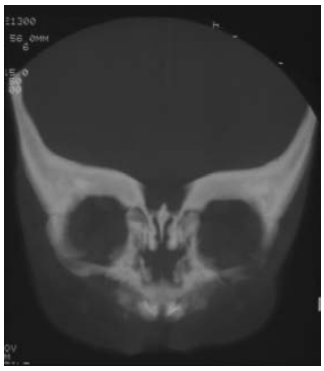
fibrils connect osteons and remodeling of woven bone to compact bone is defective.

Clinical Presentation

- ***Infantile Osteopetrosis***
  - ✓ sever form (malignant)
  - ✓ Common orofacial findings in infantile osteopetrosis

• Facial deformity (broad face, hypertelorism, snub nose and frontal bossing)
• Optic atrophy, nystagmus and blindness, deafness and facial paralysis (due to failure of resorption and remodeling of skull bones with resultant narrowing of skull foramina and pressure on various cranial nerves)
• Nasal stuffiness (due to malformation of mastoid and paranasal sinuses)
• Delayed tooth eruption
• Tooth roots often difficult to visualize due to density of surrounding bone
• Osteomyelitis as a complication of tooth extraction





- ✓ Diffusely sclerotic skeleton
  EX: Computed tomography scan indicating the extent of infantile osteopetrosis; marble-like bone occurs throughout the cranium. Compression of the optic canal results in blindness for many of these patients.
- ✓ Initial signs:
  1. normocytic anemia with hepatosplenomegaly (due to compensatory extramedullary hematopoiesis)
  2. increased susceptibility to infections (due to granulocytopenia)
  3. hydrocephalus
  4. sleep anpnea
- ✓ untreated: die during first decade of life (hemorrhage, pneumonia, sever anemia or sepsis)

- ***Adult Osteopetrosis***
  - ✓ Discovered later in life.
  - ✓ Axial skeleton → significant sclerosis
    Long bones → minimal or no defects
  - ✓ 40% are asymptomatic & marrow failure is rare.
  - ✓ Symptomatic patients : bone pain
  - ✓ Dental radiographs show a diffuse increased radiopacity of medullary bone → diagnosis
  - ✓ 2 major adult variants exist.
    → cranial nerve compression (+) ; fracture (rare)
    → nerve compression (uncommen) ; fracture (+)

✓ Common orofacial findings:

- Congenitally absent, delayed or unerupted malformed teeth
- Increased susceptibility to caries due to reduced calcium–phosphorus ratio in both enamel and dentin that may decrease hydroxyapatite crystal formation
- Most serious complication is increased susceptibility to develop osteomyelitis. As the vascular supply to the jaws is compromised, avascular necrosis and infection after dental extractions may lead to osteomyelitis.

Intermediate Osteopetrosis

- ✓ Asymptomatic at birth, frequently exhibit fractures by the end of their first decade of life.
- ✓ Marrow failure and hepatosplenomegaly are rare.
- ✓ Cranial nerve deficits, short stature, macrocephaly, mild or moderately severe anemia and ankylosed teeth(predispose to osteomyelitis of the jaws).

Transient Osteopetrosis

- ✓ Radiography reveals evidence of diffuse sclerosis and marrow failure.
- ✓ Resolve without specific therapy , return to normalcy and with no known sequelae.

Histopathologic Features

- ✓ Abnormal endosteal bone formation:
  1. tortuous lameller trabeculae replacing the cancellous portion of bone
  2. globular amorphous bone deposition in marrow spaces.
  3. osteophytic bone formation
- ✓ osteoclasts : number(+/-) ; no functional evidence (Howship's lacunae are not visible)
- ✓ Infantile form: abundant, bone surfaces; nuclei are numerous; fibrous tissue crows the marrow spaces.
- ✓ Adult form: osteoid (+) and osteoclast (few); lack ruffled borders ; numerous ; large

Differential Diagnosis

- ✓ Causes of widespread osteosclerosis : Van Buchem disease, autosomal dominant osteosclerosis (endosteal hyperostosis of the Worth type), sclerosteosis.
- ✓ Pyknodysostosis → impacted teeth
- ✓ Cathepsin-K gene defect → nonfunctioning osteoclast.
- ✓ Using the brain isoenzyme of creatine kinase (BB-CK) as a biochemical marker of osteopetrosis

Treatment and Prognosis

Adult osteopetrosis; infantile osteopetrosis ; different prognosis

Bone Marrow Transplantation

- ✓ Only permanent cure
- ✓ Remarkable improvement among many infantile osteopetrosis
- ✓ 50%; 40%; Not benefit all

Hormonal and Dietary Therapy

- ✓ Calcium-deficient diet
- ✓ Calcitriol → stimulating dormant osteoclasts (some p't resistant)
- ✓ Interferon gamma-1b, (+ Calcitriol) → reduce bone mass and decrease the prevalence of infections and nerve compression.
- ✓ Corticosteroids → increase circulating red blood cells and platelets, PTH, macrophage colony stimulating factor, erythropoietin.

Supportive Measures

- ✓ Anemia, infection
- ✓ Antibiotic therapy
- ✓ Surgical intervention/decompression
- ✓ Hyperbaric oxygen → promote healing in recalcitrant cases

Conclusion

- ✓ Special attention → fragile bone status (osteoclast function)
- ✓ Refer patients wuth osteopetrosis to a specialist for even the simplest extraction or dental surgical procedures.
- ✓ Avoid extractions in the high risk group of patients.

題號	題目
1	在下列何種情況下，牙齒仍可萌出? (A) 缺乏嗜骨細胞 (B) 無牙根 (C) 缺乏纖維母細胞 (D) 缺乏膠原纖維
答案 (B)	出處：Oral Histology (by TEN CATE; fifth edition) P292~P294; 94 年第二階國考題
題號	題目
2	下列何者不會使顎骨脆弱易於骨折? (A) 骨質疏鬆症(Osteoporosis) (B) 地中海型貧血(Mediterranean anemia) (C) 糖尿病 (D) 骨質硬化病(Osteopetrosis)
答案 (C)	出處：Oral and Maxillofacil Pathology(by Neville..; 7th edition) P503~P504; P535~P537