CHAPTER 16
BONE DISEASES

Bone, like reinforced concrete, consists of **three** main elements, and any defect in one of these elements will result in the weakening of bones. These elements are:

1. Collagen fibers type I, which represent the steel bars of concrete. Arrangement of collagen fibers will determine the type of bone.
2. Ground substance, which represents the cement of concrete and consists mainly of osteocalcin and osteonectin. The collagen fibers together with the ground substance are sometimes termed osteoid tissue.
3. Hydroxyapatite crystals of calcium phosphates, which represents the stones (cobblestone or aggregates) of concrete.

16.1 Classification of bone diseases Important

1. Developmental diseases
   (a) Facial fibrous dysplasia
   (b) Cherubism, (Familial fibrous dysplasia)
   (c) Marble bone disease
   (d) Achondroplasia
   (e) Cleidocranial dysostosis
   (f) Oxycephaly
   (g) Osteogenesis imperfecta
   (h) Hypophosphatasia
   (i) Hypophosphatemia
2. Diseases of unknown etiology
   - Paget's disease of bone
3. Inflammatory
   (a) Periapical abscess

(b) Periapical granuloma

(c) Dry socket

(d) Osteomyelitis

i. Pyogenic osteomyelitis

A. Acute pyogenic osteomyelitis

B. Chronic pyogenic osteomyelitis

ii. Chronic non-specific osteomyelitis

A. Chronic osteomyelitis with proliferative periostitis (Garre's osteomyelitis)

B. Diffuse sclerosing osteomyelitis

C. Focal scelerosing osteomyelitis

iii. Chronic specific osteomyelitis

A. Tuberculous osteomyelitis

B. Syphilitic osteomyelitis

C. Actinomycotic osteomyelitis

(e) Chemical necrosis of bones

(f) Irradiation necrosis of bones (osteoradionecrosis)

4. Tumors of bone

(a) Bone forming tumors

i. Osteoma

ii. Osteogenic sarcoma

(b) Cartilage forming tumors

i. Chondroma

ii. Chondrosarcoma

(c) Fibrous tissue forming tumors

i. Fibroma

ii. Ossifying fibroma

iii. Fibrosarcoma

iv. Giant cell tumor of bone

v. Giant cell granuloma

(d) Marrow tumors

i. Ewing's sarcoma

ii. Lymphomas

iii. Myelomas

(e) Tumors arising from entrapped cells
    i. Odontogenic tumors
    ii. Craniopharyngioma
(f) Tumors of Langerhans histiocytes (Histocytosis X group)
    i. Eosinophilic granuloma
    ii. Hand - Schuller - Christian disease
    iii. Letterer - Siewes disease
(g) Metastatic Tumors of bone

5. Cystic (Refer to the chapter "Cysts & Cyst-Like Lesions", page (109)
6. Hormonal
    (a) Hyperparathyroidism
    (b) Hypoparathyroidism
7. Deficiency diseases
    (a) Rickets
    (b) Osteomalacia
8. Metabolic diseases
    - Osteoporosis

16.2 Developmental Bone Diseases

16.2.1 Fibrous dysplasia (Maccune-Albright Syndrome) Important

Fibrous dysplasia[1] is a developmental fibro-osseous lesion. A fibro-osseous lesion is the lesion that consists of fibrous tissue intermingled with dysplastic bone trabeculae. Some controversy, still exists regarding the nomenclature of such lesions and their classifications.

Fibrous dysplasia of bone is of two types:

Monostotic

Affecting single bone, when affects one of the facial bones, it is called facial fibrous dysplasia

[1] Unlike epithelial dysplasia, fibrous dysplasia is not a premalignant or precancerous lesion

Table 16.1: Classification of Fibro-osseous Lesions

Always Remember

1. Fibrous dysplasia
2. Cemento-osseous dysplasia (osseous dysplasia)
   (a) Focal cemento-osseous dysplasia
   (b) Periapical cemento-osseous dysplasia (periapical cemental dysplasia)
   (c) Florid cemento-osseous dysplasia (florid cemental dysplasia)
   (d) Familial gigantiform cementoma
3. Ossifying fibroma, cementifying fibroma and cemento-ossifying fibroma
4. Juvenile ossifying fibroma (Juvenile aggressive ossifying fibroma)

Modified after Neville et al, [4]

Polystotic

Affecting more than one bone and are further classified into two types:

1. Jaffe type (Jaffe-Lichtenstein syndrome): characterized by polystotic fibrous dysplasia and cafe au lait pigmentation of the skin.
2. Albright syndrome (Maccune-Albright syndrome): which in addition of the above, the patient shows sexual precocity particularly in females in addition to other endocrinopathy such as hyperthyroidism or pituitary adenoma.
3. Mazabraud syndrome, characterized by fibrous dysplasia and intramuscular myxomas.

16.2.2 Facial fibrous dysplasia

A developmental monostotic fibroosseous lesion, its growth stops with cessation of skeletal growth. Fibrous dysplasia of bone belongs to an arbitrary group of lesions known as fibro-osseous lesions. Fibro-osseous lesions could be defined as lesions that consist of fibrous tissue intermingled with bone, osteoid, cementum-like or other caclific tissues. For detailed classification of fibro-osseous lesions see table (16.1). For other types of fibro-osseous lesions, see Chapter “Benign Odontogenic Tumors” and tables (13.2) and (13.3).

Etiology

- Recent data reconfirm that the disease is not hereditary; very few convincing data are present to support the hereditary basis.
- The disease results form somatic mutation in the GNAS1 gene

- The mutation occurs post-zygotically and is lethal if it occurs in the single cell zygote (incompatible with life) and is compatible with life, only when it occurs in mosaic state (Happle hypothesis) i.e. other normal cells should coexist with the mutant cells for the latter to survive.
- The extent of the damage depends upon the stage at which the zygote was affected by such mutation. In the early stages, extensive involvement of the skeletal, skin and endocrine system will occur and vice versa.
- If the mutation occurs in one of the undifferentiated stem cells (embryonic stem cells) during early embryonic life, the osteoblasts, melanocytes and endocrine cells that represent the progeny of that mutated cell all will carry that mutation and express the mutated gene. The clinical presentation of multiple bone lesions, cutaneous pigmentation and endocrine disturbances would result. If the mutation occurs during postnatal life, the progeny of that mutated cells are essentially confined to one site, resulting in fibrous dysplasia affecting a single bone.
- The mutation affects the progenitor cell of the bone marrow –stromal stem cells–. These cells also termed (colony forming unit-fibroblastic, CFU-F) can differentiate into multiple phenotypes (cartilage, fat, bone, hematopoiesis-supportive stroma and fibrous tissue).
- This result in the formation of mutated fibroblasts, which will fail to form the supportive structure needed for hematopoietic tissue and fatty bone marrow formation, instead we will find abnormal fibrous tissue in place of the normal bone marrow. Also the mutated osteoblasts will fail to from the normal lamellar bone. The collagen fibers of the new bone are perpendicular to rather than collinear to the bone-forming surface.

Clinically

- Age: 4 – 18 years
- Sex: Female more than male
- Site: Maxilla more than mandible. Usually unilateral.
- Features: Start as a hard swelling distal to the canine causing buccal swelling, proptosis of the eye, maxillary sinus obliteration, nasal obstruction, and pushing the occlusal plain of the upper teeth downward resulting in malocclusion.

X- Ray

Three patterns have been described depending on the amount of formed lesional bone. The key feature of all patterns is that the margins merge faintly with surrounding normal bone. The 3 patterns are:

1. Orange peel pattern seen in intraoral films and ground glass appearance in extra-oral films
2. Ill defined radiolucent pattern in which few faint trabeculae are seen.

3. Smoke screen pattern.

Teeth

1. Faint or ill-defined lamina dura.
2. Reduced thickness of periodontal membrane space.
3. After extraction the socket is filled with dysplasia bone.

Histologically

- Resorption of the original bone and replacement by fibrous tissue with many blood vessels.
- Then, trabeculae of osteoid are laid down and are equidistant form each other. These trabeculae are Chinese letter shaped or U, C, and W shaped.
- Osteoblastic rimming is usually absent or minimal, and peritrabecular clefting (artifactual retraction of the stroma from the bony trabeculae) is common.
- Calcification of osteoid occurs and formation of woven bone is complete. In less active lesions lamellar bone may be found.

Complications

- Rarely neoplastic changes.
- Deformity of the orbit.
- Obliteration of the maxillary sinus.

Treatment

- Plastic surgery after 20 years of age.
- Surgical correction may be required to alleviate the severe deformity before the age of 20 years

16.2.3 Cherubism (Familial fibrous dysplasia) Important

This is a developmental intraosseous fibrous swelling, its growth stops with cessation of skeletal growth. The term cherubism is derived from the word cherub, which means a child with a beautiful and chubby (rounded and plump) face similar to an angel. In theology cherub is a member of the second order of angels, often represented as a beautiful rosy-cheeked child with wings. The term Cherubism is given because of the bilateral involvement of the maxilla and or mandible, which result in the chubby and rounded appearance of the face. The term –familial fibrous dysplasia should be avoided because cherubism has no relationship to fibrous dysplasia of bone.

Etiology

- Hereditary, autosomal dominant. Penetrance in males is 100% while penetrance in females is only 50 to 70%.
- The Cherubism gene was mapped to 4p16.3. The responsible gene was named SH3-binding protein (SH3BP2). The onset of the abnormalities of Cherubism and their organ-restricted characteristics may be related to dental developmental processes in children, when signals unique to the mandible and maxilla are transmitted through the extracellular matrix, triggered by the eruption of secondary teeth.

Clinically

- Age: 2 –4 years of age.
- Sex: Males are affected more than females in a ratio of 2:1.
- Site: Mandible more than maxilla, bilateral more than unilateral. Cases were also described in which both mandible and maxilla were involved.
- Features: Bilateral firm swelling at the angle of the mandible or in the maxilla or both. When the disease occurs bilaterally in the maxilla, there is an "upward look to heaven" or "eyes upturned to heaven" appearance that is due to a wide rim of exposed sclera resulting from downward stretching of the lower eye lid by the swelling. Failure of eruption of teeth in the affected site is a common finding.

X- Ray

Well defined multilocular radiolucent area.

Histologically

Cherubism is a central giant cell lesion, it consists microscopically of:

1. Loose vascular connective tissue stroma containing mononuclear cells and areas of hemorrhage.
2. Multinucleated giant cells.
3. Little amount of bone trabeculae.
4. This picture is identical to any other giant cell lesion.

Treatment

- Plastic surgery after 20 years age.

- Surgical correction may be required to alleviate the severe deformity before the age of 20 years

16.2.4 Marble bone disease

Important

(osteopetrosis, Albers-Schönberg disease)

Definition

- Developmental bone disease characterized by decreased osteoclastic resorption of bone resulting in increased bone density.
- There are two main forms of the disease, the infantile and the adult types

Infantile osteopetrosis (malignant osteopetrosis)

- Autosomal recessive inheritance
- Congenital or starts in early childhood
- The most severe form
- Brittle bones with multiple bone fracture
- Marrow failure resulting in anemia, thrombocytopenia, leucopenia and granulocytopenia
- Compensatory hepatosplenomegaly
- Evidence of cranial nerve compression such as blindness, deafness and facial paralysis are common
- Increased susceptibility to infection
- Facial deformity, broad face, hypertelorism, snubs nose and frontal bossing
- Delayed or failure of eruption of teeth
- Difficult extraction of teeth
- Dry socket and osteomyelitis are the most common complication after dental extraction
- Delayed formation of sequestrum is the most common feature of osteomyelitis
- The prognosis is bad and the disease is fatal within the first decade of life
- Less severe variants exist and have been termed intermediate osteopetrosis

Adult osteopetrosis (benign osteopetrosis)

- Autosomal dominant inheritance
- Starts later in adult life
- Less severe than the infantile osteopetrosis

- Usually affects the axial skeleton and rarely affects long bones
- 40% of cases are asymptomatic and discovered by routine dental radiographs
- The disease is usually associated with long-term survival

Histologically:

- Replacement of spongy bone with dense compact bone
- Reduced marrow spaces
- Osteoclasts lack normal Howship's lacunae

X- Ray

- Increased radiopacities of bone to the degree that outlines of teeth are obliterated.
- Dental radiographs are useful in diagnosis due to the contrast between the shadows of teeth and bones

Treatment

- Bone marrow transplantation is the treatment of choice with a success rate of about 45%
- Because of the unavailability and risk of marrow transplantation, the following modalities may be useful
- Calcitriol
- Parathromone
- Corticosteroids
- Antibiotics
- Hyperbaric oxygen

Dental Management

- Extraction of teeth should be the last resort, conservative treatment is preferred
- Extraction, if performed should be atraumatic as possible with saucerization and suturing of sockets. The use of prophylactic antibiotics is recommended
- Osteomyelitis of the jaw needs rapid intervention to minimize bone loss
- Osteomyelitis requires pus drainage, surgical debridement, bacterial culture with sensitivity test and appropriate antibiotics

- The infection often requires prolonged antibiotic therapy with fluoroquinolones and lincomycin being most effective
- Hyperbaric oxygen is useful in promoting healing

16.2.5 Craniosynostosis

- Craniosynostosis is a generic term denoting early ossification of one or more of the cranial sutures resulting in abnormal head shape
- Skull deformity occurs due to retarded skull growth perpendicular to the affected suture associated with increased growth along the same direction that the suture follows
- Craniosynostosis is classified into primary and secondary
- Primary craniosynostosis results form abnormal suture biology and is further classified into syndromic and non-syndromic (isolated)
- Syndromic craniosynostosis occurs as a result of many syndromes, the major ones are: Crouzon syndrome, Apert syndrome, Pfeiffer syndrome and Carpenter syndrome
- Most of these syndromes show autosomal dominant inheritance
- Most of theses syndromes are due to mutations in one of the FGFR genes
- Non-syndromic (isolated form) is of unknown etiology
- Secondary craniosynostosis shows normal biology of sutures but there is abnormal internal or external forces resulting in early closure of sutures
- Secondary craniosynostosis usually results from failure of brain growth and thus results in micorcephaly
- No medical treatment exists to stop an early ossification of a cranial suture. Infants may require a series of surgical procedures to reduce the intracranial blood pressure or for cosmetic or other functional reasons

16.2.6 Achondroplasia

Developmental disease characterized by defective growth of bones developed in cartilage.

Etiology

Hereditary, autosomal dominant. Although this condition can be inherited in an autosomal dominant manner, 80% of cases are due to new, sporadic mutations. Mutations involve the gene encoding fibroblast growth factor receptor 3 (FGFR3), situated on chromosome 4. Most commonly, a point mutation causes

the substitution of arginine for glycine in the transmembrane region of the receptor. There is growing evidence that mutations of FGFR3 confer a –gain of function–. It is proposed that the normal function of FGFR3 is to slow down the formation of bone by inhibiting the proliferation of chondrocytes. Hence, the FGFR3 acts as a negative regulator of bone growth. The mutation increases the activity of FGFR3, severely limiting bone growth. This theory is supported by the knock-out mouse model in which the receptor is absent, and so the negative regulation of bone formation is lost. The result is a mouse with excessively long bones and elongated vertebrae, resulting in a long tail. Achondroplastic mouse models will be a useful tool in developing potential treatments.

Clinically

- Short legs, arms and fingers
- The trunk is of normal length
- Saddle nose
- Small maxilla (midfacial hypoplasia)
- Normal mandible
- Intelligence is normal and the patient is strong taking wrestling as a profession

16.2.7 Osteogenesis Imperfecta Important

A hereditary condition resulting from abnormality in the type I collagen, which most commonly manifests as increased fragility of bones. Four types of OI exist, based on the classifications of Sillence et al.

Etiology

- Hereditary, more than one mode of inheritance, most cases are autosomal dominant, autosomal recessive inheritance was also reported.
- The basic defect lies in the gene coding for collagen type I
- Mutations in the loci (COL1A1 on band 17q21 and COL1A2 on band 7q22.1, respectively) cause osteogenesis imperfecta
- Type I collagen fibers are found in bones, organ capsules, cornea, sclera, and meninges
- Qualitative defects (abnormal collagen I molecule) and quantitative defects (decrease in production of normal collagen I molecules) both exist

Clinically

- Dentinogenesis imperfecta in types II and III and in around 50% of patients with types I and IV
- Patients most commonly present with bone fragility.
- Prenatal ultrasound during second trimester shows bowing of long bones, fractures and limb shortening.
- Repeated fracture after mild trauma.
- Deafness (50% by age 40 years)
- Blue sclera
- Mild short stature

Histologically and histochemistry

- Decreased trabecular bone volume and thin cortices
- Reduced calcification rates and smaller apatite crystals
- Decreased collagen fibril diameter

16.3 Bone Diseases of Unknown Etiology

16.3.1 Paget's disease of bone (Osteitis Deformans)

Important

Overview

- First diagnosed by Sir James Paget in 1877, Paget's disease of bone, or osteitis deformans is a disease characterized by increased deossification associated with dysplastic reossification.
- In this disorder, the osteoclasts become abnormally activated, possibly by viral infection, and produce an irregular and distorted pattern of resorption, to which there is usually an intense osteoblastic response with irregular new bone formation often in the form of woven bone. Thus, in Paget's disease there may be increased bone density, but because of the irregular architecture, bone strength is decreased and pathologic fractures may occur. Paget disease also has a genetic component that may be linked to an osteosarcoma tumor suppressor gene. This could account for the increased risk of osteosarcoma in patients with Paget disease.

Pathology of Paget's Disease

- The initial abnormality in Paget's disease is a dramatic increase in the rate of bone resorption at areas of heightened bone remodeling.
- Pagetic osteoclasts are abnormal – approximately five times larger than normal containing an average number of 20 nuclei per cell compared with three to four nuclei in normal adult osteoclasts.
- The osteoblasts are not apparently affected, however. the extreme difference in size between the two cell types causes the intensely elevated rate of bone resorption.
- Because bone resorption triggers bone formation, the rate of bone resorption is matched by a rapid rate of bone formation. The new bone is structurally disorganized, however, resulting in an overall decrease in bone strength and an increase in susceptibility to bowing and fractures.
- In addition, the abnormal bone is marked by a high level of vascularity and an excess of fibrous connective tissue in the marrow.

Etiology

- The exact etiology of Paget's disease is obscure. Historically, the postulated etiologies of Paget's disease could be described as follows:
- Paget's view was that the disease is inflammatory due to hotness and redness of the mucosa covering the affected bone.
- Disturbance of bone vascularity was also postulated as the cause of Paget's disease.
- Viral etiology was proposed by others. Osteoclasts in Paget's disease are markedly increased in number and size, have increased numbers of nuclei per multinucleated cell, and demonstrate increased resorption capacity and increased sensitivity to 1,25-(OH)2D3, the active form of vitamin D. These cells also contain nuclear inclusions, reminiscent of those seen in paramyxovirus-infected cells, which cross-react with antibodies to measles virus nucleocapsid (MVNP) antigen.
- Hereditary background was also postulated to account for the increased incidence in certain families and or population groups.
- In about 40% of familial cases and 8% of sporadic cases, germline mutations in the sequestosome 1 gene (SQSTM1) (known as p62) have been identified. Patients with SQSTM1 mutations tend to have more severe disease than those without such mutations. SQSTM1 activates osteoclasts via the nuclear factor-kappa B (NF-κB) signaling pathway.
- Studies suggest that increased bone resorption in Paget's disease may result from increased vitamin D receptor binding affinity among osteoclasts.
- It was suggested that there is increased responsiveness of osteoclast precursors to RANKL (receptor activator of nuclear factor kappa B ligand) and decreased inhibition of RANK signaling.

- Some studies suggest that underlying defects may reside not only in osteoclasts but also in osteoblasts.

Clinically

- Age: Over 40 years.
- Sex: Male affected more than female.
- Race: More common in Anglo-Saxon ancestry. The highest rates are in the United Kingdom.
- Site: Most cases are polystotic (more than one bone is affected). Rarely the disease is monostotic (limited only to one bone). Bones usually affected are legs, vertebral column, sacrum, pelvis, skull, maxilla and mandible.
- Features: Bending of legs, kyphosis, progressive enlargement of head, enlargement of face, deafness, blindness, facial neuralgia (due to compression of cranial nerves).

Oral Manifestations

See complications of the disease.

Blood Chemistry

- Increase of alkaline phosphatase, the normal level is 3 – 13 King Armstrong units, 1.5–5 Bodansky units.
- In Page's disease of bone the level of alkaline phosphatase can reach above 200 King Armstrong units and above 250 Bodansky units.
- Normal levels of blood calcium and phosphorus.
- In patients with mild disease, total serum alkaline phosphatase may be normal. In such cases, it may be helpful to assess specialized markers:
    1. For bone formation, serum N-terminal ***propeptide*** of type 1 collagen.
    2. Or for bone resorption e.g., urinary N-terminal ***telopeptide*** of type 1 collagen.

X- Ray

1. Osteolytic stage
    (a) Osteoporosis and definite radiolucent areas.
    (b) Loss of lamina dura.
    (c) Resorption of the roots of teeth.
2. Osteoblastic stage

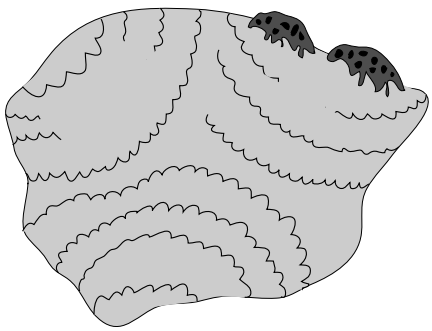


Figure 16.1: Diagrammatic representation of mosaic appearance resulting from repeated resorption of bone or cementum by osteoclasts and cementoclasts and apposition by osteoblasts or cementoblasts.

(a) New bone is laid down in a form of dense sclerotic patches giving the characteristic ***cotton wool appearance***.

(b) Hypercementosis of roots.

Histologically

- In the osteoclastic phase (bone resorption phase)
  - ⋆ Resorption of bone and replacement of marrow by highly vascular connective tissue.
  - ⋆ The osteoclasts are larger than normal with increased number of nuclei.
  - ⋆ Masses of bone which show many reversal lines giving *mosaic appearance* due to repeated resorption and apposition, see figure ((16.1)).
  - ⋆ Mosaic appearance of roots is also found.
- In Osteoblastic phase (sclerotic phase)
  - ⋆ Large masses of dense bone trabecule with many reversal lines
  - ⋆ Fibrous bone marrow

Complications

1. Heart failure due to multiple arteriovenous shunts.
2. 2 % of cases develop osteosarcoma.
3. Pathological fracture of bones.
4. Spacing of teeth.
5. Delayed sequestration.

6. Frequent remaking of dentures.
7. Difficult extraction due to hypercementosis.
8. Hemorrhage.
9. Dry socket and osteomyelitis.
10. Sever neuralgia.

Treatment

- The disease is partially controlled with calcitonin and Bisphosphonates, however the following measures should be followed:
- Good oral hygiene is mandatory to avoid complications.
- Frequent remaking of dentures to avoid bone necrosis.
- Extraction should be the last resort. Surgical extraction with minimal trauma may be necessary to avoid post-extraction complications. Suturing of extraction wounds is preferred to prevent hemorrhage and infection.
- Antibiotics before extraction.

16.4 Inflammatory Bone Diseases

16.4.1 Dry socket (Alveolar Osteitis) Important

(*Fibrinolytic Alveolitis*)

A localized osteitis affecting the lamina dura lining the tooth socket. Dry socket may be defined as that socket in which the blood clot disintegrates or fails to form, with production of foul dour without pus formation. It is the most common painful complications of dental extractions. The exact etiology of dry socket is not clear.

Predisposing factors

Many factors are blamed:

1. Infection, before, during or after extraction (active or recent history of acute ulcerative gingivitis or pericoronitis).
2. Trauma, use of excess force during extraction.
3. Local analgesia: Could be attributed to the effect of local vasoconstrictor used.

Table 16.2: Risk factors associated with dry socket

Risk factors associated with dry socket

- Previous experience of dry socket
- Deeply impacted mandibular third molar
- Poor oral hygiene
- Active or recent history of acute ulcerative gingivitis or pericoronitis associated with the tooth to be extracted
- Smoking (especially >20 cigarettes per day)
- Use of oral contraceptives
- Immunocompromised individuals

Note

4. Contamination of the socket with food, saliva and bacteria.
5. Excessive rinsing after extraction.
6. Curettage of the socket after extraction.
7. Use of oral contraceptives.
8. Paget's disease and marble bone disease.
9. General diseases as diabetes and leukemia.
10. Pathological conditions as cysts of the jaw.
11. Immunocompromized patients.
12. Table (16.2) summarizes the risk factors responsible for developing dry socket.

Pathogenesis

- The initial event is destruction of the clot which may be due to:
  - ⋆ Bacterial proteolytic enzymes.
  - ⋆ Excessive local fibrinolytic enzymes (more accepted). The alveolar bone and other oral soft tissues in particular have a high content of fibrinolytic activators (plasmin) which are released when bone is traumatized. The estrogen component of oral contraceptives enhances serum fibrinolytic activity and hence is associated with increased incidence of dry socket.
- Clot destruction leaves an open socket in which infected food and other debris accumulates in direct contact with bone which become necrotic (particularly the lamina dura)
- The necrotic bone lodges bacteria which proliferate freely, protected form leukocytes unable to reach them through this avascualr material.

- Dead bone gradually becomes separated by granulation tissue with osteoclasts and sequestra are usually shed in tiny fragments.
- Healing is by granulation tissue from the base and walls of the socket.
- The cause of pain could be attributed to the presence and formation of kinin locally in the socket. It has been shown that kinins activate the nerves, which may have already been presensitized by other inflammatory mediators.
- Plasmin is also involved in the conversion of kallikreins to kinins in the alveolar bone marrow. Thus, the presence of plasmin may give a possible explanation for the two most characteristic features of AO, namely neuralgic pain and disintegrated blood clot.

Clinically

- Three main features:
    1. Presence of bare bone
    2. Presence of pain starting 1–3 days after extraction
    3. Foul odor
- It is highly unlikely for dry socket to occur before the first postoperative day, because the blood clot contains anti-plasmin that must be consumed by plasmin before clot disintegration can take place.
- The duration of dry socket varies to some degree, depending on the severity of the disease, but it usually ranges from 5–10 days.
- Dry socket is common in the mandible than maxilla because blood supply of the mandible is lesser than that of maxilla and mandibular teeth are difficult in extraction when compared with the maxillary teeth.
- The incidence of dry socket has been reported as 3–4% following routine dental extractions and ranges from 25% to 30% after the removal of mandibular third molars.

Prevention

- Alveolar osteitis is usually unpredictable.
- Since excessive bone trauma seems to be an important predisposing factor, extraction should be atraumatic as possible.
- The prophylactic use of antibiotics is questionable and their use in routine dental extractions cannot be justified.

Table 16.3: A summary of measures to prevent the risk of dry socket

Always Remember

- Use of sound surgical practice.
- Extractions should be performed with minimum trauma.
- Confirm presence of blood clot subsequent to extraction (if absent, scrape alveolar walls gently)
- Wherever possible preoperative oral hygiene measures to reduce plaque levels to a minimum.
- Encourage the patient to stop or limit smoking in the immediate postoperative period.
- Advise patient to avoid vigorous mouth rinsing for the first 24 h post extraction.
- For patients taking oral contraceptives extractions should ideally be performed during days 23 through 28 of the menstrual cycle.

Treatment

- Irrigation with saline solution.
- Packing the socket with zinc oxide eugenol pack, Alvogel or similar dressings.
- See table (16.3) for further measures used to prevent dry socket

Complications

Osteomyelitis is the most common complication.

16.4.2 Delayed Healing of tooth socket

- Dry socket
- Irradiation on the site of extraction
- Presence of malignant tumor in the site of extraction
- Paget's disease of bone
- Marble bone disease
- AIDS
- Diabetes mellitus

16.4.3 Acute Pyogenic Osteomyelitis

Important

(Derived from Greek words osteon, meaning bone, myelo- meaning marrow, and -itis meaning inflammation)

Is the inflammation of bone and bone marrow that includes the production of pus. It is thus distinct from an osteitis such as alveolar osteitis, which is the inflammation of bone only. Also it should be differentiated from sclerosing osteomyelitis, which is characterized by proliferation of bone without pus formation.

Causative Organisms

- Anaerobic bacteria e.g. bacteroids are the usual etiologic factor.
- Sometimes Gram negative bacteria are also encountered.
- Rarely Gram positive bacteria particularly staphylococci or streptococci in contrary to osteomyelitis of long bones in which staphylococcus aureus is the most common cause.

Mode of Infection

- Dental infection, which is the most common cause e. g. periapical abscess, pericoronitis, periodontal abscess.
- Compound fracture.
- Hematogenous i. e. blood born infection as in pyemia
- Irradiation.

Pathogenesis

- Inflammation of bone will result in edema.
- As bone cannot swell, edema will occur on the expense of the blood vessels leading to collapse of these vessels (self-strangulation) and stasis of blood stream with thrombosis.
- Necrosis of the affected area will start.
- A line of separation consists of granulation tissue will appear around the necrotic area on the expense of vital bone as an attempt to localize the infection.
- Once the necrotic area is separated from the normal bone it is termed sequestrum.
- Pus, formed by liquefaction of necrotic soft tissue and inflammatory cells may escape through multiple sinuses called cloacae.
- The sequestrum will undergo gradual resorption.
- New bone will occur under the periostium and is termed involucrum.
- Where bone has died and been removed, healing is by granulation tissue which is gradually replaced by new bone.
- The sequestrum is porous, light in weight and color.

Clinically

- Rise of temperature, particularly in the early stages.
- Severe, throbbing, deeply-seated pain
- The affected area is swollen due to inflammatory edema.
- Numbness of the lower lip may occur if the inflammation spread to the inferior alveolar nerve.
- Teeth are tender and may become loose with pus may ooze from an open socket or gingival margins.
- When pus is formed it discharges through multiple sinuses into the mouth or the skin. Once pus is formed acute osteomyelitis is termed chronic osteomyelitis.
- Regional lymphadenopathy occurs.
- Osteomyelitis is common in the mandible more than the maxilla due to its poorer blood supply and due to the fact that the bone of the mandible is denser than that of maxilla.
- Osteomyelitis of maxilla is rare and is usually due to surgical interference in acute sinusitis, severe maxillo-facial injury or irradiation.

Histologically

- Dead bone (sequestrum) is recognized histologically by lacunae empty of osteocytes.
- The periphery of the sequestrum show eroded outline due to osteoclastic resorption.
- Sequestrum is surrounded by granulation tissue heavily infiltrated with acute and chronic inflammatory cells with areas of pus formation.

Blood Picture

In acute stage there is leukocytosis (increase in white blood cells).

X-Ray

- In the first two weeks no changes could be detected in the radiographic films.
- Later on irregular radiolucent areas indicating bone resorption and formation of separating lines are evident. Such radiolucent lines are usually described as moth-eaten appearance or worm eaten appearance. Subperiosteal bone formation may be seen. The sequestrum is slightly more radiopaque than normal bone, probably due to over-calcification caused by the long standing inflammatory condition (dystrophic calcification).

Complications

- Numbness of lower lip.
- Pathological fracture.
- Ankylosis of TMJ.
- Pyaemia or septicemia is rare now except in immunocompromised patients.

Treatment

- Antibiotics.
- Drainage of pus.
- Remove the source of infection such as remaining roots or foreign body.
- Monitoring good oral hygiene.
- Extraction of loose teeth.
- Removal of sequestrum when it is completely separated.
- Hyperbaric oxygen is useful in persistent cases.

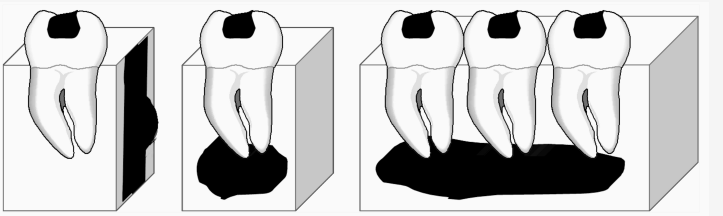
16.4.4 Chronic Pyogenic Osteomyelitis Important

- Chronic osteomyelitis may develop without any apparent acute episode (de novo) and may be due to an exceptionally low-grade infection or high local resistance. The infection is localized but persistent because bacteria growing in dead bone are inaccessible to the host defenses. Clinically and radiographically it is similar to acute osteomyelitis in its terminal stages. There is bone destruction and granulation tissue formation with little suppuration.
- Chronic osteomyelitis is subdivided into secondary chronic osteomyelitis (SCO) and primary chronic osteomyelitis (PCO), depending on the severity of the initial symptoms. SCO is defined as chronic osteomyelitis that develops secondary to acute symptoms and PCO is defined as chronic osteomyelitis that starts insidiously, with no acute phase.
- It is difficult, however, to differentiate existent lesions according to the severity of the initial symptoms. The borderline between SCO and PCO is vague and cannot be determined objectively.

16.4.5 Chronic Non-pyogenic Osteomyelitis Important

Chronic non-pyogenic osteomyelitis is characterized by bone formation resulting in the increased density of bone (sclerosis). Figure (16.2) illustrates the basic differences between the 3 types of chronic non-pyogenic osteomyelitis.

Always Remember



Different types of chronic osteomyelitis shown diagrammatically, Garres osteomyelitis (left) the reaction is subperiosteal. Focal sclerosing osteomyelitis (middle) the reaction is central and is limited to a single tooth. Diffuse sclerosing osteomyelitis (right) the reaction is central and involves several teeth.

Figure 16.2: The 3 basic types of chronic non-pyogenic osteomyelitis

Chronic Osteomyelitis with Proliferative Periostitis

(Garre's osteomyelitis, Periostitis Ossificans)

- This is a rare reaction, usually to periapical infection in young patients.
- Young individuals are more prone to be affected because of their high resistance, increased local blood supply, and greater bone regenerative capabilities.
- The newly formed bone is deposited under the periosteum on the surface of the affected bone.
- A non-tender or rarely tender bony swelling will appear usually in the mandible.
- Radiographically is characterized by the presence of lamellae of newly formed periosteal bone outside the cortex, giving the characteristic appearance of ***"onion skin"***.
- Treatment of the causative infection will result in resolution.

Diffuse Sclerosing Osteomyelitis

- A condition in which intrameullary bone proliferation occurs resulting in sclerosis
- The condition is of obscure nature and probably results from low-grade non-pyogenic infection. *Actinomyces* combined with *Eikenella corrodens* are accused as being the causative agents. These organisms are normal inhabitants of the oral flora, they become pathogens upon gaining an entry into bone. Their portal of entry may be via spread from severe periodontal disease.
- The condition shows some similarities to gigantiform cementoma and hence it was thought to be a variant of the latter. However, as the condition is usually associated with severe periodontal disease, the infective nature is postulated.

- **Clinically**, persistent ***intense pain***. Mild expansion of the mandible, and even soft tissue swelling "active exacerbation,". The mandible is usually affected more than the maxilla and mostly in the body, angle, and ramus area. The mandible may be tender to palpation, particularly at the buccal cortex. No suppuration is noted.
- **Radiographically**, it shows areas of diffuse or nodular sclerosis resembling the cotton wool appearance of Paget's disease of bone.
- **Microscopically**, shows masses of bone with many reversal lines (mosaic appearance) and infiltration with many chronic inflammatory cells and fibrosis of the marrow.
- Treatment is by removal of the source of infection and antibiotics for long period of time. Patients may relapse from an antibiotic-induced remission because the bone sclerosis limits drug penetrance.

Focal sclerosing osteomyelitis

- This is a rare form of bone reaction to periapical infection and may cause mild pain.
- The condition thus represents a localized form of the diffuse sclerosing osteomyelitis.
- The reaction is basically proliferation of bone in response to mild bacterial infection leading to bone formation rather than destruction. It is usually seen as a sclerotic area related to the apex of a dead tooth in a young patient. Mandibular teeth are affected more than maxillary teeth.
- Extraction or root canal treatment of the infected tooth should lead to resolution of the infection.
- Microscopically, there is a dense mass of bony trabeculae with minimal marrow.

16.4.6 Medication-related Osteonecrosis of the Jaw (MRONJ) Definitions Only

(Antiresorptive-related Osteonecrosis, (ARONJ))

Definition

- Medication-related osteonecrosis of the jaw (MRONJ) is a pathological condition associated with treatment using antiresorptive and/or antiangiogenic therapy for the modulation of bone remodeling. The initial reports associated MRONJ to bisphosphonates, medications that work as bone-modifying agents. Later, other agents such as the antiangiogenics, have also been reported to cause the oral complication, either alone or in combination with antiresorptives.
- These medications are used to treat osteoporosis or various malignancies that involve bone e.g., multiple myeloma, metastatic breast carcinoma, and prostate carcinoma. Less frequent uses include treatment for Paget's disease, osteogenesis imperfecta, rheumatoid arthritis, and giant cell tumors of bone.

- The majority of cases of osteonecrosis occurs in the jaw bone. Extra-gnathic bones are affected but to a far lesser extent. Cases have been reported in the ear and femur. The exact cause for such a phenomenon is not known and might be related to the selective deposition of the drugs in the skeleton.
- The majority of cases results from the intravenous use (94%), while the remaining 6% of cases results in patients taking the drug orally.

Required characteristics for the diagnosis of medication-related osteonecrosis of the jaw (MRONJ)

1. Current or previous treatment with antiresorptive or antiangiogenic agent
2. Exposed bone in maxillofacial region for longer than 8 weeks
3. No history of radiation therapy or obvious metastatic disease to the jaws

Risk factors for developing MRONJ:

1. High-concentration intake of bone antiresorptive agents, such as bisphosphonates and denosumab
2. Age
3. Duration of drug intake
4. Tooth extractions, especially when teeth have severe inflammation conditions
5. Chemotherapy
6. Corticosteroids
7. Smoking
8. Periapical and periodontal disease
9. Ill-fitting dentures
10. Traumatic occlusion

Incidence

- The mandible is involved in 65% of cases, the maxilla in 27%, and both jaws in 8%.
- In patients with exposed bone, 16% were asymptomatic, 84% were painful.
- In some cases the necrosis can lead to development of a cutaneous or mucosal sinus or pathologic fracture.
- It should be noted that the clinical, radiographic and histopathological features of all medication-related osteonecrosis are very similar.

Staging of medication-related osteonecrosis of the jaw:

1. Stage 0: No exposed necrotic bone but with associated clinical or radiographic changes such as unexplained odontalgia, dull bone pain, sinus pain, altered neurosensory function, unexplained loose teeth, sinus tracts or alveolar bone loss not associated with periapical or periodontal infection, patchy zones of osteosclerosis, thickening of the lamina dura, failure to remodel extraction sites.
2. Stage 1: Asymptomatic exposed necrotic bone or sinus tract that probes to bone
3. Stage 2: Symptomatic exposed necrotic bone or sinus tract that probes to bone associated with pain and erythema in the region with or without purulence.
4. Stage 3: Symptomatic exposed necrotic bone or sinus tract that probes to bone with more than one of the following: necrotic bone beyond the alveolus (extension to inferior border or ramus of mandible, extension into the sinus or zygoma of the maxilla), pathologic fracture, extraoral sinus tract, oral antral or nasal communication.

Causative agents, see figure (16.3):

1. Antiangiogenic agents
   (a) Tyrosine kinase inhibitors
   (b) Monoclonal antibody inhibiting vascular endothelial growth factor
2. Antiresorptive agents and bone metabolism modifiers:
   (a) Aminobisphosphonate antineoplastics
   (b) Denosumab antineoplastic
   (c) Aminobisphosphonates for osteoporosis
   (d) Denosumab for osteoporosis
   (e) Romosozumab for osteoporosis

Pathogenesis of medication-related osteonecrosis:

The pathogenesis of medication-related osteonecrosis (MRONJ) is not entirely clear, but multiple factors may be involved in specific microenvironments. Here are some possible mechanisms that have been proposed based on the search results:

1. Inhibition of angiogenesis: Antiresorptive agents and antiangiogenic agents may interfere with the normal process of angiogenesis, which can lead to impaired blood flow and tissue damage.
2. Suppression of bone turnover: Antiresorptive agents may suppress bone turnover, which can lead to accumulation of microdamage and reduced bone healing capacity.

3. Alteration of the immune response: Antiresorptive agents may alter the immune response in the oral cavity, leading to impaired wound healing and increased susceptibility to infection.
4. Disruption of the TGF-β1 signaling pathway: The TGF-β1 signaling pathway may have a key role in the development of MRONJ.
5. Reduced viability, growth, and migration of cells in the bone and soft tissues: In vitro studies have shown that reduced viability, growth, and migration of cells in the bone and soft tissues may be causative for MRONJ.

It is important to note that the pathogenesis of MRONJ is complex and likely involves multiple factors. Further research is needed to fully understand the underlying mechanisms and develop effective prevention and treatment strategies.

Radiographically:

1. In early stages, increased radiopacity of the crestal portions of each jaw (particularly the alveolar ridges), with a more normal appearance of the bone away from tooth-bearing portions.
2. In advanced stages, moth-eaten and ill-defined radiolucency with or without central radiopaque sequestra (a feature that mimics osteomyelitis).

Histopathological feature:

1. Biopsy of vital bone reveals irregular trabeculae of pagetoid bone, with adjacent enlarged and irregular osteoclasts that often demonstrate numerous intracytoplasmic vacuoles.
2. Specimens of severely affected areas reveal trabeculae of sclerotic lamellar bone, with loss of osteocytes from their lacunae and frequent peripheral resorption with bacterial colonization. Although the peripheral bacterial colonies often resemble actinomycetes, the infection is not supportive of a diagnosis of invasive cervicofacial actinomycosis.

Bisphosphonates Bone Necrosis (BON)

- Bisphosphonates are a class of drugs that prevent the loss of bone density, used to treat osteoporosis and similar diseases. They are the most commonly prescribed drugs used to treat osteoporosis.
- The drug is also used in the treatment of Paget's disease of bone, bone metastasis, multiple myeloma, primary hyperparathyroidism, osteogenesis imperfecta, fibrous dysplasia, and other conditions that exhibit bone loss.
- This drug may lead to surgical complication in the form of impaired wound healing following oral, periodontal surgery or endodontic therapy.

- The majority of cases appear to result from intravenous bisphosphonate therapy (94%). Only the remaining 6% of cases arose in patients taking bisphosphonates orally.
- In the serum, 50% of bisphosphonates is cleared rapidly by the kidneys with the remainder going to bone.
- The mode of action is not yet completely understood, it is hypothesized that the condition is related to a defect in jaw bone physiologic remodeling or wound healing. The strong inhibition of osteoclast function precipitated by bisphosphonate therapy can lead to inhibition of normal bone turnover. Because bisphosphonates are preferentially deposited in bone with high turnover rates, it is possible that the levels of bisphosphonate within the jaw are selectively elevated.
- A diagnosis of bisphosphonate-associated osteonecrosis of the jaw relies on three criteria:
  - ⋆ Current or history of bisphosphonate medication.
  - ⋆ Area of exposed bone in the jaw persisting for more than 8 weeks.
  - ⋆ No history of radiation therapy to the head and neck.
- There is presently no known prevention for bisphosphonate-associated osteonecrosis of the jaw.
- **Precautions:** Similar to that of osteoradionecrosis. See page (340)

Antiangiogenic therapy bone necrosis

- A correlation was found between the use of antiangiogenic therapy and osteonecrosis of the jaw.
- The antiangiogenic agents are prescribed for a variety of malignancies and include tyrosine kinase inhibitors and monoclonal antibodies directed against vascular endothelial growth factor.
- This risk is increased if these agents are combined with bisphosphonates.

Monoclonal antibody against osteoclastic maturation

- It was found that there is a correlation between the use of monoclonal antibody designed to prevent osteoclastic maturation (denosumab) and the incidence of osteonecrosis of the jaw.
- Denosumab is a monoclonal antibody that reduces osteoclastic function, but it does this by inhibiting osteoclastic differentiation. This medication quickly reduces osteoclastic activity by 85% with maximal reduction occurring within 1 month of an injection.
- The medication is not deposited in bone and has a half-life of 24.5 days, with complete clearance in 4 to 5 months.

16.4.7 Irradiation Necrosis Important

(Osteoradionecrosis)

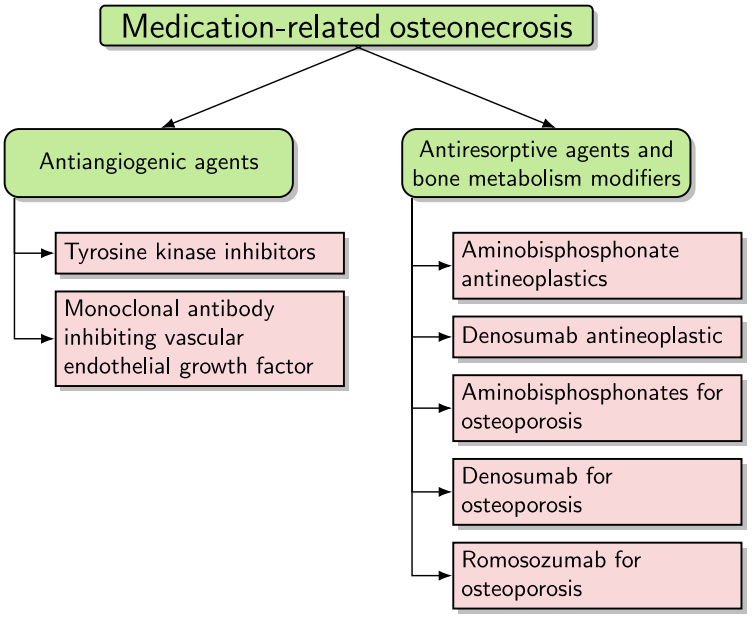


Figure 16.3: Medication-related osteonecrosis of the jaw.

Is the necrosis or decreased vitality of bone due to irradiation.

Etiology

- **Historical**: In luminal dial painters.
- Nowadays the most usual cause is radioactive isotopes used in the treatment of malignancy without good protective measures.

Pathogenesis

Irradiation will result in:

1. Endarteritis obliterans.
2. Death of osteoblasts and osteocytes.
3. This will result in necrosis of bone or at least decreased vitality, which allow easy infection.

Clinically

Similar to pyogenic osteomyelitis but there is prolonged course with delayed sequestration.

Irradiation also will result in:

- Delayed eruption of teeth or exfoliation of tooth germs.

- Stunted teeth.
- Asymmetry of face duo to affection of the mandibular growth centers.

Precautions

- Improvement of dental health to prevent future procedures that disrupt bone; this includes elimination of foci of infection and removal of partially impacted teeth, loose teeth and remaining roots.
- Conservative treatment of teeth is preferred in irradiated jaws.
- Extraction or surgery is contraindicated unless special preparation of the patient is done. These preparation includes antibiotic prophylaxis starting one day before and extending 3 days after any invasive dental procedure.

16.5 Tumors of Bone

16.5.1 Compact and Cancellous Osteoma

See chapter “Benign Non-Odontogenic Tumors & Tumor-Like Lesions”, page (179)

16.5.2 Osteoid Osteoma

See chapter “Benign Non-Odontogenic Tumors & Tumor-Like Lesions”, page (180)

16.5.3 Ossifying Fibroma

Ossifying fibroma and its related disorders (cementifying, cemento-ossifying fibroma) are discussed in the chapter “Benign Odontogenic Tumors”, page (263)

16.5.4 Central Giant Cell Granuloma Important

(Central giant cell reparative granuloma)

A lesion of unknown nature, it may represents unusual reaction of bone against unknown irritant. It was thought that the lesion is a local reparative process, hence the name reparative was proposed.

Clinically

- Appears clinically as a slowly growing painless swelling.
- Age: Usually below 20 years of age.
- Site: Mandible is affected more than maxilla. Usually in the molar region.

X- Ray

Multilocular radiolucent area.

Histologically

Similar to any giant cell lesion it consists of:

- Loose vascular connective tissue rich in mononuclear cells thought to be fibroblasts.
- Multinucleated giant cells which are found usually around areas of hemorrhage. They are formed by fusion of neighboring cells or by division of the nucleus without division of the cytoplasm. The origin of these cells is thought to be histiocytes, osteoclasts or stromal cells.
- Little amount of bone trabeculae.

Treatment

- Surgical enucleation
- In recurrent or aggressive cases, more radical surgery
- Intralesional injection of corticosteroids (particularly, triamcinolone acetonide) weekly for 6 weeks
- Systemic calcitonin by intradermal injection or by intranasal spray daily for 12 months
- Interferon alpha was also tried with variable success rate

16.5.5 Giant Cell Tumor of Bone (Osteoclastoma) Important

A tumor of bone of variable clinical behavior, some cases are of low-grade malignancy with no metastasis while others are of high-grade malignancy and do metastasize to the lungs.

Clinically

- The lesion affects old age groups usually at 40 years of age.

- It occurs at the ends of long bones and very rarely in the jaws (epiphysis). This lesion appears clinically as a painful rapidly growing swelling that destroys the affected bone and can metastasize to remote areas (about 15% of cases).

X - Ray

Radiographically giant cell tumor of bone appears as an aggressive radiolucent area.

Histologically

The microscopic picture of giant cell tumor of bone is similar to any giant cell lesion except for the presence of abnormal mitosis, nuclear pleomorphism and hyperchromatic nuclei. The lesion consists of:

1. Loose vascular connective tissue stroma rich in mononuclear cells thought to be fibroblasts. The cells are plump shaped showing criteria of malignancy.
2. Multinucleated giant cells which are more large than those of giant cell granuloma.
3. No or very little bone formation.

Treatment

Hemiresection, yet recurrence is common unless the tumor is adequately removed during surgery.

16.5.6 Tumors of Langerhans Cell Histiocytes Important

(Histocytosis X group)

Definition

This group of lesions commonly involves bone, although it is not primarily a tumor of bone. The cell of origin of this group of lesions is believed to be the Langerhans cell of the surface epithelium. This cell is of bone marrow origin and is a member of the mononuclear phagocystic system MPS. The cell is S-100 protein positive. An alternative name of Langerhans histiocytosis was proposed for this group of lesions instead of the older term histiocytosis X.

The pathogenesis is unknown. An ongoing debate exists over whether this is a reactive or neoplastic process.

Arguments supporting the reactive nature of this disorder include

- The occurrence of spontaneous remissions

- The failure to detect aneuploidy, metaphase or karyotypic abnormalities
- The good survival rate in patients without organ dysfunction.

support for the neoplastic origin for this proliferation

- The infiltration of organs by aberrant cells
- A possible lethal evolution
- Successful treatment using cancer-based modalities

Classification

LCH can affect various organs and tissues in the body, and it can present in different forms and severities. Here is a general classification for Langerhans cell histiocytosis:

A newer classification of Langerhans cell histiocytosis is as follows:

1. **Unifocal** – The old term was eosinophilic granuloma.
2. **Multifocal unisystem** – Hand-Schüller-Christian triad.
3. **Multifocal multisystem** – Letterer-Siwe disease.

A more recent classification is as follows:

1. Single-system single site **(SS-s)** – eosinophilic granuloma.
2. Single-system multi-site **(SS-m)** – Hand-Schüller-Christian triad.
3. Multisystem type **(MS)** – Letterer-Siwe disease.

Eosinophilic granuloma Important

Eosinophilic granuloma represents the most benign form of epidermal cell Langerhans histiocytosis.

Clinically

- Eosinophilic granuloma affects young age, usually below 10 years.
- The lesion is usually solitary, rarely multiple. Flat bones are commonly affected rarely long bones or soft tissues. In the jaws eosinophilic granuloma appears as a painful swelling associated with inflammation of the area and looseness of the teeth.

X- Ray

Radiographically eosinophilic granuloma appears as an area of complete radiolucency (***punched out radiolucent area***).

Histologically

The microscopic picture of eosinophilic granuloma is a mass of granulation tissue with eosinophils and histiocytes.

Treatment

Curettage.

Prognosis

The prognosis of this lesion is very good.

Hand–Schüller–Christian Disease Important

Hand–Schüller–Christian disease represents the moderate form of Langerhans cell histiocytes group.

Clinically

- This lesion is common in young age - below 6 years.
- It consists of triad of symptoms that includes:
    1. Exophthalmos because the lesion occurs behind the eye and displace the eyeball.
    2. Diabetes insipidus, because the lesion occurs in the sella tursica and then replace the posterior pituitary which secretes the antidiuretic hormone.
    3. Multiple affection of bones and if the jaw bones are affected it produces painful swellings with inflammation and loose teeth.

X- Ray

The radiographic picture of Hand–Schüller–Christian disease is similar to that of eosinophilic granuloma.

Histologically

Microscopically the lesion is composed mainly of granulation tissue, histiocytes, eosinophils and foam cells. The presence of foam cells is diagnostic for this disease.

Treatment

No effective treatment.

Prognosis

The prognosis of this disease is bad.

Letterer-Swie Disease Important

Letterer–Swie's disease represents the most dangerous form of Langerhans cell histiocytes.

Clinically

- This lesion is common in infants below 2 years of age. It is a multiple disease affecting many bones.
- Hepatomegally, splenomegally, enlargement of lymph nodes, anemia and thrombocytopenia are common clinical signs of this disease. The patient might complain of erythematous skin rashes.

Histologically

The lesion appears microscopically as granulation tissue with histiocytes replacing the normal tissues.

Prognosis

The prognosis of this disease is bad, it is usually fatal.

16.6 Hormonal bone diseases

16.6.1 Hyperparathyroidism Important

(Von-Recklinghausen's disease of bone, Osteitis fibrosa cystica)

Is the over secretion of parathromone (parathyroid hormone).

Types

1. Primary: Which is due to adenoma or hyperplasia of the gland.
2. Secondary: Which is due to renal failure.
3. Rarely, occurs as a part of some inherited syndromes, e.g. multiple endocrine neoplasia type 1 or type 2a, or hyperparathyroidism–jaw tumor syndrome. In the latter condition, affected patients develop multiple jaw lesions that histopathologically are consistent with central ossifying fibroma with increase risk of developing parathyroid carcinoma.

Action of parathormone

The action of parathormone is to elevate calcium level of the blood through:

1. Activation of osteoclastic activity.
2. Decrease phosphate reabsorption in the kidney.
3. Increase calcium reabosrption in the kidney.

Blood Chemistry

- Serum calcium level is increased.
- Serum phosphorus level is decreased.
- Alkaline phosphatase is increased.
- Urinary output of calcium is increased.

Clinically

- Sudden cardiac arrest might occur due to hypercalcemia.
- Renal failure due to multiple renal stones.
- Hypertension and heart failure due to renal failure.
- Pain in the back and extremities.
- pathological fracture of bones.

Pathogenesis

Generalized resorption of bone and replacement by new bone poorer in calcium. Sometimes, a failure of bone formation occurs instead, granulation tissue with multinucleated giant cells is formed. This granula-

tion tissue appears radiographically as radiolucent masses and hence the term *osteitis fibrosa cystica* was given.

X- Ray

1. Generalized osteoporosis with ground glass appearance best seen in the jaw because teeth are used as a marker.
2. Loss of lamina dura.
3. Sometimes areas of complete radiolucency appear and are termed *osteitis fibrosa cystica.* At the time of the operation, these areas appear brown due to excess hemosiderin pigments and are termed *brown nodes of hyperparathyroidism.*

Histologically

- The bone marrow is replaced by granulation tissue.
- Brown nodes are similar to any giant cell lesion and consist of spindle shaped cells with many multinucleated giant cells and areas of hemorrhage.

Treatment

- Primary hyperparathyroidism, the treatment is partial or total parathyroidectomy.
- Secondary hyperparathyroidism, the treatment is kidney transplant.

16.7 Deficiency Diseases

16.7.1 Rickets Important

Is a deficiency disease that occurs between 6 months and 2 years and the changes persist throughout life.

Etiology

Deficiency of calcium, phosphorus or vitamin D. Other rare cause of rickets is the excess fluorides in drinking water. The excess fluorides can interfere with the proper formation of bone and teeth

Blood Chemistry

Low phosphorus level, low calcium level and elevated serum alkaline phosphatase.

Clinically

Rickets is characterized clinically by deformity of long bones, delayed closure of fontanels, thin and flat cranial bones (***craniotabes***), delayed eruption of teeth, enamel and dentin hypocalcification and open bite.

Histologically

Osteoblasts continue to lay down excess soft bone matrix with deficient calcification.

Treatment

- Adequate diet rich in calcium and phosphorus such as milk.
- Calcium, Phosphorus and vitamin D supplementation.

16.7.2 Osteomalacia Important

Is the adult form of rickets and occurs usually in women associated with pregnancy and lactation due to increased demand for calcium.

Blood Chemistry

Low Phosphorus level, low calcium level and elevated serum alkaline phosphatase.

Clinically

Osteomalacia is characterized clinically by Deformity of legs and pelvis, deformity of vertebral column leading to pain due to compression of the spinal nerves. The jaws are rarely affected, however cases have been described in which increased mobility of teeth occurring during pregnancy were noticed in the absence of any inflammatory gingivitis or periodontitis. Such mobility may be attributed to the softness of the alveolar bones supporting the teeth due to marginal deficiency of calcium associated with pregnancy.

Treatment

As in the cases of rickets.

16.8 Metabolic Bone Diseases

16.8.1 Osteoporosis Defintion only

Definition

Is defined as low bone mass with a normal ratio of mineral to osteoid (the organic matrix of bone). Bone mass increases until approximately age 30 and then gradually declines. Both men and women experience an age-related decline in bone mass density (BMD) starting in midlife. Women experience more rapid bone loss in the early years following menopause. Diagrammatic representation of osteoporosis is illustrated in figure ((16.4))

Classification

Osteoporosis can be classified into primary and secondary:

1- Primary Osteoporosis

- Primary osteoporosis is the most common metabolic disorder of the skeleton.
- Can be classified into type 1, or postmenopausal osteoporosis, and type 2, or senile osteoporosis.
- However, recent studies have suggested that estrogen deficiency is important for the pathogenesis of both types of osteoporosis and in both men and women.
- Primary osteoporosis can occur in both genders at all ages but often follows menopause in women and occurs later in life in men.
- Primary osteoporosis is often called the "***silent disease***" because bone loss occurs without symptoms. People may not know that they have osteoporosis until their bones become so weak that a sudden pathological bone fracture occurs.
- The loss of bone mass and strength can be contributed to:
    1. Failure to reach an optimal peak bone mass as a young adult.
    2. Excessive resorption of bone after peak mass has been achieved.
    3. Decreased bone formation during remodeling.

- The rate of bone formation is inadequate to replace the bone lost by resorption. This could be because of a defect in osteoblast function. The defect in osteoblast function could be the consequence of cellular senescence, or a decrease in the synthesis or activity of systemic and local growth factors.

2- Secondary Osteoporosis

- Secondary osteoporosis occurs as a result of prolonged corticosteroid therapy, hypogonadism, and immobilization (prolonged recumbency).

Osteoporosis and alveolar bone loss

- It has been confirmed that there is decreased thickness of the mandibular alveolar process in the first premolar region.
- Studies have also shown that age-related bone loss is greater in women than men after the age of 50 years.
- These findings may possibly explain the findings in several surveys of dental health that women tend to lose their teeth earlier.

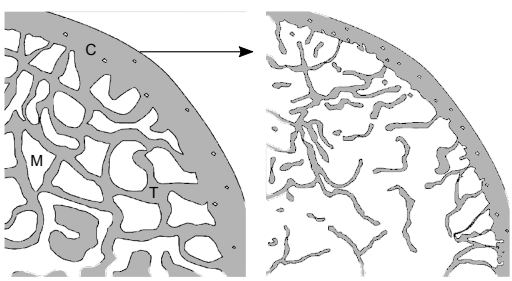


Figure 16.4: Diagrammatic representation of osteoporosis. Left panel represents normal bone structure while the right panel represents the osteoporotic bone with thin bone trabeculae (T), cortex (C) and wide marrow spaces (M).