
Osteopetrosis –A rare inherited disorder- A case report

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Abstract

Osteopetrosis is a disorder with defective function of osteoclasts. It is a congenital condition, which means people are born with it. The most common symptoms are bone fractures, low blood cell levels, impaired vision and hearing, and dental problems related to infection. Dentists should be aware of patients with the disease because of its effect on osteoclast function. Care should be taken for these patients to maintain oral health as well as general health as their condition makes them more vulnerable for frequent infections and fractures. The purpose of this paper is to emphasize the signs and symptoms as well as differential diagnosis of osteopetrosis and to provide guidance to dentists on the management of patients with osteopetrosis.

Keywords: Osteopetrosis, Osteosclerosis, Autosomal recessive, Autosomal dominant.

1. Introduction

Osteopetrosis is a clinical syndrome characterized by the failure of osteoclasts to resorb bone, also known as marble bone disease and Albers-Schonberg disease. As a consequence, bone modeling and remodeling are impaired. The defect in bone turnover characteristically results in skeletal fragility despite increased bone mass, and it may also cause hematopoietic insufficiency, disturbed tooth eruption, nerve entrapment syndromes, and growth impairment. Overall incidence of osteopetrosis is estimated to be 1 case per 100,000-500,000 population. It takes 2 major clinical forms- the autosomal dominant adult (benign) form is associated with few or no symptoms and the autosomal recessive infantile (malignant) form, if untreated, is typically fatal during infancy or early childhood. [1]

A rare autosomal recessive (intermediate) form presents during childhood with some signs and symptoms of malignant osteopetrosis may exist as lethal, transient infantile and post infectious forms. Most children born with the malignant form of osteopetrosis die during infancy. Due to better medical care the life expectancy of these patients has increased in recent years. Most studies of osteopetrosis have concentrated on medical aspects (hepatosplenomegaly, anemia, increased susceptibility to infections most common is respiratory tract infections, cardiac disorders, multiple fractures etc.). [2] With increasing age, however, dental

development and tooth eruption become a practical and medical problem. [3] In these patients to improve oral hygiene, especially in areas of exposed mandibular bone, 0.2% chlorhexidine formulations can be used. Fluoride applications can be done to decrease the susceptibility to dental caries. [4]

2. Case report

A 43 years old female came to the dept. of oral surgery complaining of pain in lower jaw and missing teeth. No relevant history of hypertension, asthma, tuberculosis, drug allergy, bleeding disorders, cardiovascular disease. History of anemia and is under medication since 5 years with iron supplements.

Patient also gives history of oral infection and associated illness and hospitalization 5 years back and was treated with IV antibiotics for 15 days. No relevant surgical history. Patient gives history of traumatic extraction 5 years back in the right lower back teeth due to caries and was followed by severe infection in that area and the wound did not heal for one month. She was treated in the hospital for 15 days during which she underwent surgical debridement of the wound. Her parents are apparently healthy. She has one sister and she is apparently healthy. On clinical examination patient was calm, co-operative and well oriented with normal built

and moderately nourished. There were no detectable systemic diseases present.

Extra orally there is facial asymmetry in the right side of the face with scar in the lower border of the mandible. One right submandibular lymph node is palpable, tender, firm in consistency measuring around 1.5cm x 1.5 cm in size, freely mobile. Mouth opening restricted with Interincisal distance of 35mm. Jaw movements were normal. Teeth missing were 15,16,27,31,32,33,34,35,41,42,43,44,45,46,47. (Fig-1) Urine and blood routine investigations revealed normal results.

OPG reveals presence of surgical plating in relation to 36, 37 periapical regions, 4cm discontinuity in the lower cortical region of the mandible in the left premolar region. (Fig-2) Resected mandible leaving 1cm cortical border in the right side of the mandible, thickening of the fractured edges in the right body of the mandible with interposed 0.5cm radiolucency between the fractured edges also seen. Radiograph of hands and legs reveals the obliteration of the normal marrow spaces with increased radio opacity of bone depicting a “Candle stick appearance.” (Fig- 3)

Radiograph of pelvic bone also reveals increased radio opacity of the bone with healing fracture site in the left femur which also denotes the site of mal union due to malposition of the fracture edges. (Fig-4)

Histopathological examination of buccal cortical specimen from extracted 37 region reveals dense sclerotic bone with most of the marrow spaces replaced with bone. The bone is avascular with some islands of cartilage.

The confirmatory test would be using brain iso-enzyme of creatine kinase which is a biochemical marker of osteopetrosis. Considering the above features the patient was diagnosed as a case of marble bone disease or osteopetrosis.



Figure 1- Intra oral missing tooth



Figure 2: OPG shows fracture and resection



Figure 3: X-ray of legs showing increased radio opacity

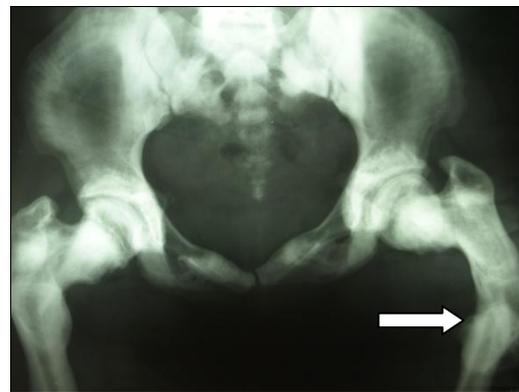


Figure 4: X-ray of pelvic bones showing fracture

3. Discussion

Normal bone growth is achieved by a balance between bone formation by osteoblasts and bone resorption (break down of bone matrix) by osteoclasts. In osteopetrosis, the number of osteoclasts may be reduced, normal, or increased. Most importantly, osteoclast dysfunction mediates the pathogenesis of this disease. The exact mechanism is unknown. However, deficiency of carbonic anhydrase in osteoclasts is noted. The absence of this enzyme causes defective hydrogen ion pumping by osteoclasts and this in turn causes defective bone resorption by osteoclasts, as an acidic environment is needed for dissociation of calcium hydroxyapatite from bone matrix. Hence, bone resorption fails while its formation persists. Excessive bone is formed.[1]

Despite this excess bone formation, people with osteopetrosis tend to have bones that are more brittle than normal. Mild osteopetrosis may cause no symptoms, and present no problems. However, serious forms can result in stunted growth, deformity, increased likelihood of fractures, also patients suffers anemia, recurrent infections and hepatosplenomegaly due to bone expansion leading to bone marrow narrowing and extramedullary hematopoiesis. It can

also result in blindness, facial paralysis, and deafness, due to the increased pressure put on the nerves by the extra bone. [2]

With increasing age, however, dental development and tooth eruption become a practical and medical problem.[3] In these patients to improve oral hygiene, especially in areas of exposed mandibular bone, 0.2% chlorhexidine formulations can be used. Fluoride applications can be done to decrease the susceptibility to dental caries. [4]

Table 1: Clinical Classification of Human Osteopetrosis[4]

| Characteristic | Adult onset | Infantile | Intermediate |
|---------------------|--------------------|---------------------|---------------------|
| Inheritance | Autosomal dominant | Autosomal recessive | Autosomal recessive |
| Bone marrow failure | None | Severe | None |
| Prognosis | Good | Poor | Poor |

Dental abnormalities may be attributed to the pathological changes in osteopetrosis. Patients with the disease seem to be especially susceptible to caries. Constriction of canals housing neurovascular bundles that supply teeth and jaws, along with obliteration of the marrow cavities and the dental pulp chambers, is the most likely contributing factor to bone necrosis and dental caries. Other dental changes may include delayed eruption and early loss of teeth, enamel hypoplasia, malformed roots and crowns, and thickening of the lamina dura. [5]

It has a bactericidal and bacteriostatic effect in vitro and in vivo but the bone infection is not the only factor but reduced tissue resistance due to avascularity of the marrow spaces and the partial obliteration of the mandibular canal appeared to be the basic problem. The beneficial effect is probably resulted from the improved vascular supply and increased oxygen perfusion to the ischemic areas of infection. It is a potentially severe infection that runs a protracted course, due to the accompanying severe anemia and neutropenia. [6]

Bony encroachment of the cranial nerve foramina leads to cranial nerve palsies and optic atrophy with blindness and deafness. Their bones are susceptible to fracture. Most patients fail to grow and death occurs at an early age, as a result of severe chronic anemia, bleeding and/or infection. [7]

Abnormal bone formation and fibrous tissue replace the bone marrow space and finally hematopoiesis is decreased. Extramedullary hematopoiesis occurs resulting in leukoerythroblastic anemia and thrombocytopenia. Liver and spleen enlarge progressively. Hemolysis resulting from hypersplenism worsens the anemia and thrombocytopenia.[8] Genetic consultations are important. Prenatal diagnosis of osteopetrosis early in pregnancy is an indication for termination of the pregnancy. [9][10]

3.1 Differential diagnosis

The differential diagnoses include other disorders which can cause diffuse osteosclerosis, such as hypervitaminosis D, and hypoparathyroidism, [11] Paget's disease, diffuse bone metastasis of breast or prostate cancer (which tend to be osteoblastic while most metastases are

osteolytic) intoxication with fluoride, lead or beryllium, and hematological disorders such as myelofibrosis, sickle cell disease and leukemia. [12]

3.2 Treatment:

Medications administered in osteopetrosis include the following:

- Vitamin-D supplements - Appear to help by stimulating dormant osteoclasts, thus stimulating bone resorption
- Corticosteroids - Have also been used to stimulate bone resorption and to treat anemia
- Erythropoietin - Another agent that can be used against anemia
- Gamma interferon - Improves white blood cell function, greatly decreasing the incidence of new infections [3]

Both the adult and childhood forms of osteopetrosis may benefit from Actimmune injections. Actimmune (interferon gamma-1b) delays the progression of malignant infantile osteopetrosis because it causes an increase in bone resorption (breakdown of old bone tissue) and in red blood cell production.

In this case oral prophylaxis was done and oral hygiene measures instituted. There was loss of support of previous denture due to resected bone in the left side of the mandible. [11] Opinion from Dept. of prosthodontics was obtained regarding the replacement of the missing teeth. Patient was referred to general hospital regarding Bone marrow transplantation treatment.

4. Conclusion

Special attention should be paid to patients with osteopetrosis due to their fragile bone status resulting from defects in osteoclast function and consequent impaired wound healing. Proper prenatal screening for the genetic disorder followed by maintenance and supportive therapy can help the patient to lead a near normal life. These patients should receive increased attention and prophylactic dental treatment to maintain their fragile oral health status. Preventive measures must be continuously and vigorously maintained.[11][12] Dentists should refer patients with osteopetrosis to a specialist for even the simplest extraction or other surgical dental procedures to ensure management of the serious adverse effects that may arise from oral surgery.

References

- [1] Lam DK, Sándor GK, Holmes HI, Carmichael RP, Clokie CM. "Marble bone disease: a review of osteopetrosis and its oral health implications for dentists". *J Can Dent Assoc* 2007; 73 (9): 839–43.
- [2] Philip J Sapp. *Contemporary Oral and Maxillofacial pathology*. 2nd edition.110-111.
- [3] Van Hove RP, de Jong T, Nolte PA. Autosomal dominant type I osteopetrosis is related with iatrogenic fractures in arthroplasty. *Clin Orthop Surg*. 2014 Dec. 6(4): 484-8.

- [4] Beighton P, Hamersma H, Cremin BJ. Osteopetrosis in South Africa. The benign, lethal and intermediate forms. *S Afr Med J.* 1979 Apr 21; 55(17): 659-65.
- [5] Baron R. Anatomy and Ultrastructure of Bone. Favus MJ, ed. *Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism.* 4th ed. Philadelphia, Pa: Lippincott, Williams, and Wilkins; 1999. 3-10.
- [6] Tolar J, Teitelbaum S, Orchard PJ. "Osteopetrosis". *New England Journal of Medicine* 2004; 351 (27): 2839–49.
- [7] Kjell Bjorvatn, Ole Gilhuus-Moe and Dagfinn Aarskog; Oral aspects of osteopetrosis; *Scand. J. Dent. Res.* 1979; 87: 245-252.
- [8] Dick HM, Simpson. J Dental changes in osteopetrosis. *Oral Surg* 1972 sept; 34:408. Lawoyin DO, Daramola JO, Ajabge HA, Nyako EA, Lawoyin JO. Osteomyelitis of the mandible associated with osteopetrosis: Report of a case. *Br J of oral and max surg.* 1988; 26:330-5.
- [9] Jalevik B, Fasth A, Dahllof G. Dental development after successful treatment of infantile osteopetrosis with bone marrow transplantation. *Bone Marrow Transplant* 2002; 29: 537-40.
- [10] Gerritsen EJA, Vossen JM, Van Loo IHG, et al. Autosomal recessive osteopetrosis: variability of findings at diagnosis and during the natural course. *Pediatrics* 1994; 93(2):247-53.
- [11] Besbas N, Draaken M, Ludwig M, et al. A novel CLCN7 mutation resulting in a most severe form of autosomal recessive osteopetrosis. *Eur J Pediatr* 2009; 168(12): 1449-54.
- [12] Barba MF, Doria AS, Torre MB, Nakano EK, Kim CA, Andrade MR, Bogus LCN, Scatigno Neto A. Osteopetrosis—two cases report and image diagnostic. *Pediatrics.* 1995; 17: 60–63.