

Residual Cyst in Osteopetrosis- Unveiling the Enigma!!

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I. Introduction

Osteopetrosis refers to a group of rare, inherited skeletal disorders characterized by increased bone density due to a defect in remodeling caused by the failure of normal osteoclast function. Also known as marble bone disease, Albers-Schonberg Disease, OsteosclerosisFragilisGeneralisata¹.

The estimated prevalence of osteopetrosis is 1 in 100,000 to 500,000. Osteopetrosis is caused by mutations in at least 10 genes with inheritance of autosomal recessive(osteopetrosiscongenita) , autosomal dominant(osteopetrosistarda), or X-linked recessive and the most severe form being autosomal recessive which is characterized by carbonic anhydrase II deficiency, renal tubular acidosis and cerebral calcification.²

The adult form is milder than the other forms, and may not be diagnosed until adolescence or adulthood when symptoms first appear. Symptoms of the adult type of osteopetrosis include osteosclerosis, fractures usually of the ribs and long bones, osteomyelitis especially mandible, cranial hyperostosis, diaphyseal sclerosis. In some cases, affected individuals may have periapical pathology or may be asymptomatic.³

Carious exposure of dental pulps leading to osteomyelitis is a recognized complication and may contribute to the early death of the patient.

The present article documents an incidentally diagnosed case of osteopetrosistardain a 60-year-old male with residual cyst in anterior maxillary region. The importance of routine radiography is emphasized with a need for prompt care to avoid complications that might result in significant mortality in such patients.

II. Case Report

A 60 year old male patient, manual laborer reported to our dental institute with a chief complaint of slowly progressing swelling and occasional pain in relation to upper front teeth region of two weeks duration. He had noticed the swelling two weeks back due to intermittent pain. Significant alteration in the size of the swelling nor any secondary manifestations were not noticed. Dental history revealed extraction of decayed upper front teeth around two years back and had undergone multiple extractions in the past, which were all uneventful His medical history was unremarkable except for frequent headaches, lethargy, and moderate deafness in right earsince 40 years of age. He had sought consultation in our unit as the pain and swelling did not resolve on analgesics.

General examination revealed short stature, genu varum(Figure 1) and waddling gait. On extraoral examination, there was enlargement of the middle third of face, prominent supraorbital ridge, and deviated septum. Intraoral examination revealed an enlarged and symmetrical edentulous maxillary arch with root stump of 26and partially edentulous mandibular arch with 32 36 46 48. A localized softfluctuant tendercystic swelling of size 1.5 x 1.8 cm was palpable in relation toanterior maxillary region, extending from 0.5 cm away from anterior maxillary alveolar ridge to 2.5 cm posterior withnormal overlying smooth mucosa. (Figure 2)

III. Investigations

Maxillary topographical occlusal view

Revealed awell defined ovoid unilocular radiolucency of size 2 x 2.5 cm in the mid-anterior region of maxilla extending 0.5cm away from alveolar ridge to 2.5cm inferior. Radiolucency is surrounded a sclerotic rim and is superimposed over the nasal septum. Malformed crowns of the multiple impacted teeth is seen around the radiolucency. Marked homogenous opacification with altered trabecular pattern is seen over the entire exposed maxillary region. (Figure 3)

Panoramic radiograph revealed hyperostosis of the endosteal surface of maxillary cortex, increasing toward midline. A zone of more densely homogenous opaque bone adjacent to the inferior cortex was seen with a greater degree of involvement toward the anterior body of mandible , and diminishing involvement toward the obtuse mandibular angle.Thickenedshorttrabeculations with diminished and prominent marrow spaces were noted, and the walls of the inferior alveolar canal and antrum appeared to have increased thickness. Generalised

thickening of lamin dura were seen around 48 46 32 36 . Furcation involvement was noted in relation to 36 and widening of periodontal space around 33. Multiple impacted teeth were seen in relation to 16 23 24 34 35 44. Encroachment into bilateral floor of maxillary sinus, rounded patches of radioopacity simulating cotton wool appearance in relation to maxillary alveolar ridge. (Figure 4)

Paranasal sinus view

Mild hyperostotic involvement of vault and cranial base, with discrete areas of increased density in frontal area resulting from endosteal thickening of inner table. Uniform thickening of calvaria with loss of the diploic space was noted. Cranium exhibits a homogenous amorphous density and simulate a ‘‘ bladder of lard’’ appearance.(Figure 5)

The patient was advised for CT, PET scan but he was unwilling for CT or PET, as he was poor and had financial constraints.

Routine laboratory investigations and biochemical investigations were within normal limits except for the elevated acid phosphatase. Fine needle aspiration revealed turbid brown-coloured fluid, consisting dense infiltrate of acute inflammatory cells, predominantly polymorpho nuclear luekocytes. Few isolated epithelial cells were seen, which were normal in size, shape and appearance. Cytological picture was suggestive of an acute inflammatory lesion. On the basis of clinical, radiological and analysis of aspirate, a provisional diagnosis of an infected residual cyst in relation to anterior maxillary edentulous region and a diagnosis of osteopetrosis was arrived at. The differential diagnosis considered for residual cyst in anterior maxillary region included nasopalatine cyst and for osteopetrosis included sclerosteosis.

After surgical enucleation and biopsy, histopathological picture revealed non-keratinised stratified squamous epithelium with long irregular rete ridges showing the characteristic arcading pattern. (Figure 6) The underlying connective tissue was loosely fibrocellular with chronic inflammatory infiltrate containing predominantly lymphocytes and plasma cells. Many newly formed blood vessels with areas of haemorrhage were seen. (Figure 7) Histological findings confirmed clinical diagnosis of a residual cyst.

IV. Discussion

Osteopetrosis was first reported in 1904 by the German radiologist Albers-Schonberg. The term osteopetrosis was described by Karshner in 1926.⁴

Classical osteopetrosis exhibits a vast spectrum of clinical, physiologic, and genotypic expressions and has been classified into three clinically distinct forms : (1) infantile malignant autosomal recessive form, (2) intermediate mild autosomal recessive form, and (3) adult benign autosomal dominant form.⁵ One of the most common complication following tooth extraction or trauma in osteopetrosis, is the susceptibility of developing osteomyelitis in the mandible followed by maxilla owing to its thin cortical bone pattern and rich collateral blood supply.²

Pathogenesis

The causative gene has been mapped to chromosome 1p21. Although the number of osteoclasts is often increased, the defective osteoclastic bone resorption along with continued bone formation and endochondral ossification leads to cortical bone thickening and cancellous bone sclerosis. The causes of osteoclast failure are unclear, but may involve abnormalities in the osteoclast stem cell or its microenvironment, osteoblast precursor cells or the mature heterokaryon or in the bone matrix. Alterations in the factors required for bone resorption, such as the synthesis of abnormal parathyroid hormone (PTH) or defective production of interleukin-2 (IL-2) or superoxide, are also possible causes. Ultimately, impaired bone resorption results in skeletal fragility because fewer collagen fibrils connect osteons properly, and remodeling of woven bone to compact bone is defective.⁶

Adult Osteopetrosis

The adult form exhibits less severe manifestations with major involvement in the axial skeleton characterized by significant sclerosis. Approximately 40% of those affected are asymptomatic. In symptomatic patients bone pain is more frequent. Craniofacial skeletal changes can result in frontal bossing, hydrocephalus, macrocephaly, facial deformity, and choanal stenosis. Cranial nerve foramina may be narrowed by excessive development of cranial bones, resulting in deafness, visual disturbance and palsy. Malformation of paranasal sinuses occurs due to impaired resorption and remodeling process, resulting in stuffy nose. Orthopedic problems include bone pain (26%), fractures (40%) coxa vara, long bone bowing, hip and knee degenerative arthritis and osteomyelitis.

Occasionally, diagnosis may be based on dental radiographs that show a diffuse increased radiopacity of medullary bone resulting in altered teeth morphology and inhibition of tooth eruption.⁷ Dental manifestation may include increased susceptibility to caries due to compromised hydroxyapatite crystal formation. Other dental

changes may include enamel hypoplasia, teeth with malformed crown and short root, impacted teeth, Delayed eruption and early exfoliation of teeth, and thickening of lamina dura.⁸ 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 osteomyelitis. Osteomyelitis, due to dental caries (10%), is well recognized hazard in osteopetrosis. Bjorvatnet *al* demonstrated severe malocclusion of primary and permanent dentition with significant decrease in vertical growth of alveolar ridge.⁹

Standard biochemical indices of mineral homeostasis usually unremarkable, but serum acid phosphatase enzyme and parathyroid hormone levels may be elevated.¹

Radiographic features include uniform increase in the bone density without corticomedullary demarcation. The long bones exhibit a dense chalk like appearance with an 'Erlenmeyer flask' deformity at their ends due to failure of metaphyseal remodeling. Fractures are usually transverse and heal with normal callus. Bowing of the long bones as well as coxa vara may be present due to multiple fractures, There is also an increase in density of bone at the base of skull especially prominence in the floor of anterior cranial fossa. The sphenoidal and frontal sinuses and mastoids may be underpneumatized. Neural foramina may be encroached upon. The vertebral column has a 'sandwich' or 'ruggerjersey' appearance with dense sclerotic bone at each end plate of the vertebral body. A 'bone within bone' or endobone phenomenon may be seen in small bones of the hands but, with increased density around the periphery.

Differential Diagnosis

Other causes of widespread osteosclerosis may include Van Buchem disease, endosteal hyperostosis of the Worth type, and sclerosteosis. In addition, pyknodysostosis is associated with impacted teeth and nonfunctioning osteoclasts in the setting of a cathepsin-K gene defect.

It has been suggested that bisphosphonate therapy can induce a condition similar to that found with osteopetrosis. Whyte and colleagues described a case of abnormal bone remodeling and increased bone density with histologic features of osteopetrosis associated with extended pamidronate therapy in a 12-year-old boy. Such cases of BRONJ could be differentiated from osteopetrosis using the brain isoenzyme of creatine kinase (BB-CK), which is a biochemical marker of osteopetrosis.¹⁰

Some alternative diagnoses include fluorosis, beryllium, lead and bismuth poisoning, myelofibrosis, Paget's disease (sclerosing form), hypoparathyroidism and malignancies (lymphoma, osteoblastic cancer metastases). The diagnosis of osteopetrosis is based on radiological and clinical features and these findings in this case suffice to make a definite diagnosis of osteopetrosis.¹¹

Treatment and Prognosis

Although the diagnosis of osteopetrosis is straightforward, mostly based on typical radiographic appearance, the management is complex and a major challenge for the clinician. Adult osteopetrosis is usually associated with long-term survival as this form of the disease is mild. However, the prognosis for infantile osteopetrosis without therapy is usually poor, with most of those affected dying in their first decade of life. Due to the differing severity of the various forms of osteopetrosis, a correct diagnosis is prudent before proper therapy can be initiated.¹²

Bone Marrow Transplantation

Bone marrow transplantation is the only permanent cure for osteopetrosis, but an appropriately matched donor is usually available for only about 50% of those affected, and engraftment is successful in about 45% of transplants. Bone marrow transplantation may result in remarkable improvement among many infantile osteopetrosis patients, but may not benefit all because of the varying underlying causes of the disease.¹³

Hormonal and Dietary Therapy

Interferon gamma-1b, often in combination with calcitriol, has been shown to reduce bone mass and decrease the prevalence of infections and nerve compression. Calcitriol may help by stimulating dormant osteoclasts, but some patients are resistant to this treatment. Other therapies include corticosteroids to increase circulating red blood cells and platelets, PTH, macrophage colony stimulating factor and erythropoietin.¹⁴

Supportive Measures

Osteomyelitis requires rapid intervention with early diagnosis, drainage, debridement, bacterial culture and sensitivity testing followed by appropriate antibiotic therapy. Hyperbaric oxygen may be useful to promote healing in recalcitrant cases.¹²

V. Conclusion

A proper clinical, hematological & radiological investigation will help to arrive at the definitive diagnosis in a case of osteopetrosis. Treatment is symptomatic and genetic counseling & reassurance should be given to the patient. Special focus should be given to these patients with osteopetrosis due to their fragile bone status resulting from defects in osteoclast function and consequent impaired wound healing.