International Journal of Contemporary Pediatrics
Kumar N et al. Int J Contemp Pediatr. 2023 Feb;10(2):248-251
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20230094

Case Report

Radiological signs in osteopetrosis

Nitish Kumar*, Tanya Singh

Department of Pediatrics, ABVIMS and Dr. RML Hospital, New Delhi, India

Received: 29 November 2022
Accepted: 03 January 2023

***Correspondence:**
Dr. Nitish Kumar,
E-mail: doctornitishkumar@gmail.com

ABSTRACT

Osteopetrosis, or marble bone disease, is a rare genetic metabolic bone disease initially described by Albers-Schönberg in 1904. Osteopetrosis includes a clinically heterogeneous group of conditions characterized by increased bone density due to a defect in bone resorption by osteoclasts. The osteoclasto-genesis as well as the osteoclastic activity may be distorted. Clinical symptoms of osteopetrosis vary greatly in their presentation and severity as the spectrum ranges from the neonatal onset with life-threatening complications to incidental findings of osteopetrosis on radiographs. Diagnosis is based on clinical and radiographic evaluation, confirmed by bone biopsy and genetic testing. Treatment depends on the symptoms and severity of the disease and requires a multidisciplinary team approach.

Keywords: Osteopetrosis, Osteoclastogenesis, Marble bone disease

INTRODUCTION

Osteopetrosis, or marble bone disease, is a rare genetic disorder described by Albers Schönberg in 1904. Literature mentions 1 in 250 000 births for ARO and 1 in 20 000 births for ADO.[1] Osteopetrosis includes a clinically heterogeneous group of conditions characterised by increased bone density due to a defect in bone resorption by osteoclasts. This results in excessive deposition of immature bone, thickening of the cortical bones, and failure of the outgrowth of spaces in the cranial vault.[2]

Mutations in many different genes have been identified. Osteopetrosis may be inherited in autosomal dominant osteopetrosis (ADO) or the adult type, autosomal recessive osteopetrosis (ARO), malignant infantile type, or X-linked recessive pattern.[1]

CASE REPORT

Clinical symptoms of osteopetrosis vary greatly in their presentation and severity. The spectrum ranges from the neonatal onset with life-threatening complications (due to bone marrow failure) to incidental findings of osteopetrosis on radiographs.[1] The increased bone mass paradoxically weakens the bone thus with an enhanced predisposition to fractures and osteomyelitis. Also, the expanding bone may narrow nerve foramina causing deafness, blindness, facial palsy, swallowing difficulties, and atrophy of the retina. Severe dental caries, dental abscesses, or delayed tooth development are also common, as well as growth retardation/failure and delayed psychomotor development.[3] ARO, the most severe type, is associated with diminished life expectancy and is fatal if untreated. Symptoms of ARO appear soon after birth and may present with early and late-onset neonatal sepsis.[4]

Diagnosis

Diagnosis is based on clinical and radiographic evaluation, confirmed by bone biopsy and genetic testing. The bone biopsy can distinguish between osteoclast-poor and -rich subtypes.

Therapy

Management depends on the symptoms and severity of the disease and requires a multidisciplinary team approach. The best therapeutic approach for patients with ARO is allogeneic hematopoietic stem cell transplantation (HSCT).[5] Interferon gamma-1b has been tried in non-responder to HSCT or as a bridging therapy to transplantation.[6] The prognosis is poor in absence of HSCT, most children die in early childhood due to anaemia, infections, and bleeding manifestations.[1]

Written informed consent for the publication of the clinical details and clinical images was obtained from the parents.

An 11-year-old male child was admitted with complaints of bilateral ear discharge (left>right) on and off since childhood and deviation of mouth to the right side in the past 3 days. Ear discharge was yellow in colour, profuse, mucopurulent, foul smelling and blood-tinged associated with hearing loss. Deviation of mouth was insidious in onset, gradually progressive associated with slurring of speech and drooling of saliva. The child has a significant history of fractures of bones of the hand and leg in infancy without adequate stress. Antenatal and postnatal history was uneventful. There was no H/o blood transfusion, consanguinity or similar family history.

On physical examination, the child had short stature, a macrocephalic head with frontal bossing, and hepato-splenomegaly. The ophthalmic evaluation revealed visual acuity: Right eye PL +ve, PR inaccurate; Left eye FC at 2 meters, PR accurate. B/L EOM has restrictions in abduction and adduction and nystagmus is present. Anterior segment WNL. Bilateral eye showing optic atrophy on fundus study. Diffuse swelling of the preauricular and postauricular region involving the mastoid was present thus ear examination and rhinoscopy was done suggesting B/L ear discharge and polyp in left EAC; grade 4 adenoid hypertrophy respectively. Audiometry reported bilateral conductive hearing loss.

Lab investigations: Hb 12 g/dL, white blood cells 8.9 k/uL, and platelet count 3.2 lakh, and ESR in the normal range. Peripheral smear showed normocytic and normochromic anaemia. Renal function and serum electrolytes were within normal limits (creatinine 0.32 mg/dL, sodium 136 mEq/L, and potassium 3.9 mEq/L). Liver function tests were normal (serum bilirubin 0.26 mg/dL, SGOT 21 IU/L, SGPT 18.3 IU/L, alkaline phosphatase 149 IU/L, total protein 7 gm/L, albumin 4.6 gm/L, globulin 3 gm/L) serum calcium-9.4 mg/dL (reference-range: 8.5-10.5), phosphorus-3.5 mg/dL (reference range: 2.5-4.5). Vitamin D3 level 27.4 ng/dl, PTH 45.7 pg/ml. Serum alkaline phosphatase, thyroid hormone, parathormone, iron studies, and vitamin B12 levels were within normal range. Intra-oral examination revealed the presence of incomplete permanent dentition, constriction of maxilla with grooved palate causing crowding, and mandibular arch showed the presence of irregularly placed teeth. Dental caries involving pulp with gross destruction of the clinical crown are seen radiographically.

Metaphyseal cupping and fraying on X-ray of long bones while ‘sandwich vertebral body sign-on X-ray spine was noted. The base of the skull and orbits were thickened and sclerosed elucidating ‘Goggle sign’ and paranasal sinuses were poorly pneumatized.

NCCT showed bony outgrowth from the inner table of the left temporal bone with underlying soft tissue swelling suggesting sequelae of B/L chronic osteomyelitis.

CECT PNS

Soft tissue thickening was seen in bilateral middle ear cavities with symmetrically increased density of skull bones and narrowing of skull base foramina (rotundum, ovals, spinous and lacerum). These findings are suggestive of osteopetrosis with a close differential of Paget’s disease of the skull.

The patient was treated with antibiotics and steroids and supplemented with vitamin D and calcium. As reviewed on regular follow-ups at our paediatric endo. OPD anaemia in osteopetrosis is leuko-erythroblastic in type. Constricted cranial foramina lead to multiple cranial nerve palsies.

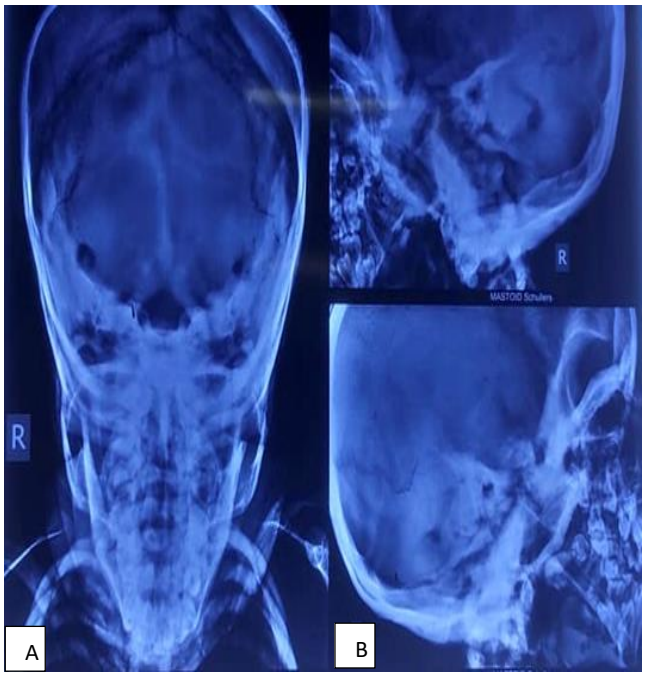

Figure 1 (A and B): Radiograph X-ray skull and neck of constriction of maxilla with grooved palate with crawled irregularly placed teeth. Lateral radiograph of neck with mastoid and base of skull thickened and sclerosed elucidating ‘Goggle sign’.

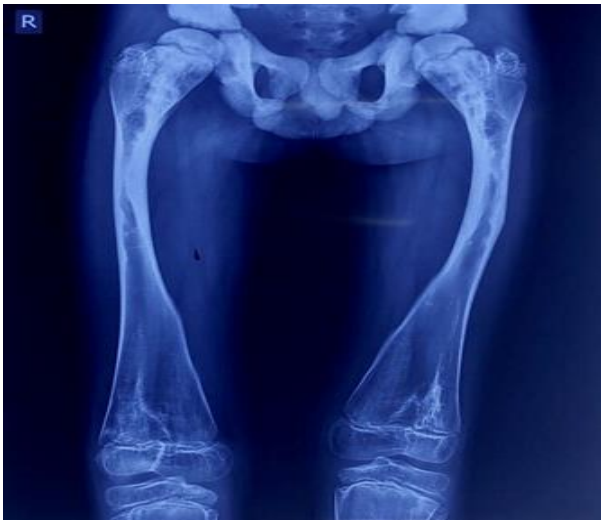

Figure 2: Radiograph of long bones showing metaphyseal cupping and fraying depicting erlenmeyer flask bone deformity.

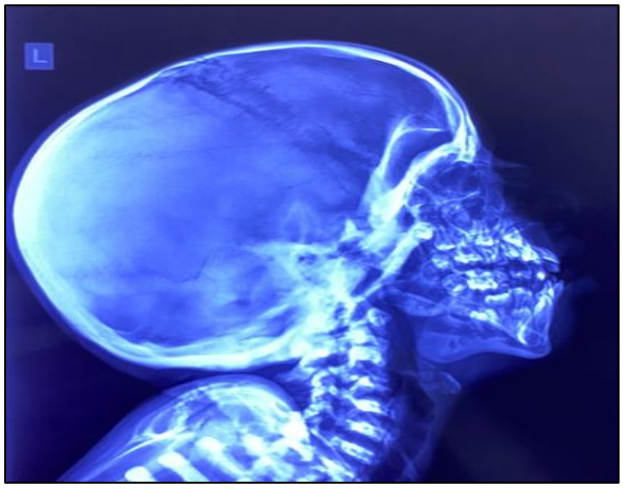

Figure 3: X-ray skull lateral view reveals calvarial and basilar thickening and sclerosis, with poorly developed sinuses and mastoid process.

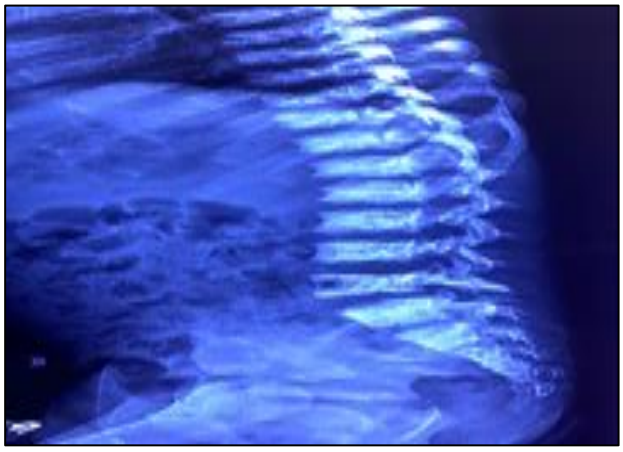

Figure 4: X-ray spine of sandwich vertebral body sign.

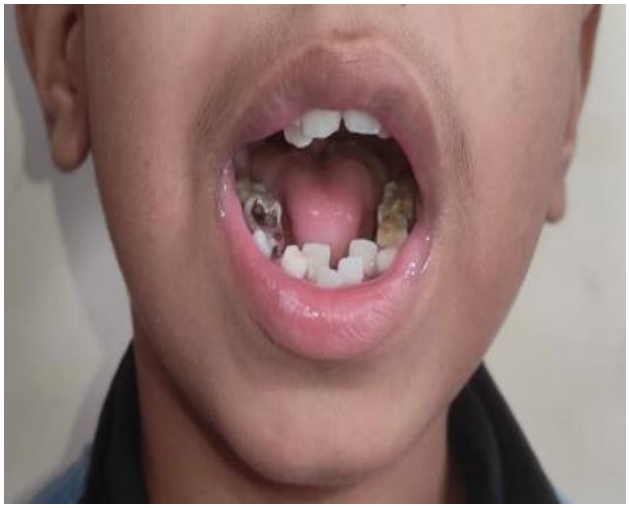

Figure 5: Oral cavity showing mandibular arch with irregularly placed crowded teeth and dental caries.

DISCUSSION

Osteopetrosis is an inherited connective tissue disease resulting in abnormally dense bones prone to fracture. This metabolic bone disorder comprises a group of conditions that share the hallmark of increased bone density on radiographs.[3] The increase in bone density results from impaired osteoclast differentiation or function. Four forms of the disease have been identified, (a) an autosomal dominant benign heterogeneous form, (b) an autosomal recessive severe malignant form, (c) an intermediate form that is a recessive type, and (d) a recessive type with renal tubular acidosis (also known as carbonic anhydrase II deficiency syndrome).[1]

Clinical features include severe anaemia, bleeding episodes and infections, hepatosplenomegaly, lymphadenopathy, frequent pathological fractures from minor trauma, and failure to thrive.[7]

Radiological findings are classical and include generalized sclerosis of the skeleton with homogeneously increased density of all the bones with little or no differentiation between cortical and medullary regions. While the bones may appear dense and thick, they are brittle and subject to pathological fractures. The skull shows basilar and calvarial thickening and poorly developed sinuses.[8]

Dental abnormalities include caries, delayed eruption and early loss of teeth, enamel hypoplasia and malformed roots and crowns.[9] Osteopetrotic patients are prone to develop infections and are susceptible to jaw bone fractures and osteomyelitis which is a potentially severe infection that runs a protracted course, due to the accompanying severe anaemia and neutropenia.[10] Surgical resection should be planned with caution as the osteoporotic bone has less capacity to heal and these children are at risk of adverse respiratory events and increased perioperative morbidity and mortality as

anaesthetic complications.[11] Treatment regimens include systemic antibiotics coupled with thorough debridement of necrotic bone and primary closure of soft tissues.[12]

CONCLUSION

Osteopetrosis, a rare metabolic bone disease, may run a severe protracted course with generalized involvement of hematological and skeletal system. Hence, early diagnosis through characteristic radiological clues can aid in preventing the irreversible complications.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Stark Z, Savarirayan R. Osteopetrosis. Orphanet J Rare Dis. 2009;4(1):1-2.
2. De Cuyper E, De Cuyper C, Willems L, Casselman J, Dhooge I, Van Hoecke H. Hearing Loss in Malignant Infantile Osteopetrosis: A Case-Based Review. J Int Adv Otol. 2021;17(6):551.
3. Föger-Samwald U, Dovjak P, Azizi-Semrad U, Kerschan-Schindl K, Pietschmann P. Osteoporosis: Pathophysiology and therapeutic options. Excli J. 2020;19:1017.
4. Gillani S, Abbas Z. Malignant infantile osteopetrosis. J Ayub Med College Abbottabad. 2017;29(2):350-2.
5. Penna S, Villa A, Capo V. Autosomal recessive osteopetrosis: mechanisms and treatments. Dis Models Mech. 2021;14(5):dmm048940.
6. Yadav S, Chalise S, Chaudhary S, Shah GS, Gupta MK, Mishra OP. Osteopetrosis in two siblings: two case reports. BMC Res Notes. 2016;9(1):1-4.
7. Raman Gangadha RS, Prakashchandra SP, Rupal P. Osteopetrosis with Typical Radiological Findings: Rare Case Report. Int J Anat Radiol Surtg. 2015;4:36-8.
8. Boulet C, Madani H, Lenchik L, Vanhoenacker F, Amalnath DS, De Mey J et al. Sclerosing bone dysplasias: genetic, clinical and radiology update of hereditary and non-hereditary disorders. Bri J Radiol. 2016;89(1062):20150349.
9. Arumugam E, Harinathbabu M, Thillaigovindan R, Prabhu G. Marble bone disease: a rare bone disorder. Cureus. 2015;7(10).
10. Bedi RS, Goel P, Pasricha N, Goel A. Osteopetrosis-A rare entity with osteomyelitis. Ann Maxillofacial Sur. 2011;1(2):155.
11. Sözen T, Özışık L, Başaran NÇ. An overview and management of osteoporosis. Eur J Rheumatol. 2017;4(1):46.
12. García CM, García MA, García RG, Gil FM. Osteomyelitis of the mandible in a patient with osteopetrosis. Case report and review of the literature. J Maxillofacial Oral Surg. 2013;12(1):94-9.

Cite this article as: Kumar N, Singh T. Radiological signs in osteopetrosis. Int J Contemp Pediatr 2023;10:248-51.