Case Report

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Osteopetrosis with Typical Radiological Findings: Rare Case Report

Radiology Section

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ABSTRACT

Osteopetrosis is a rare hereditary bone disorder characterized by overgrowth and sclerosis of bone due to faulty bone remodelling. Clinical features include severe anemia, repeated infections and fractures, hepatosplenomegaly, and cranial neuropathies due to entrapment. On X-ray there is generalized increased in density of the bones, which are devoid of trabeculations and appreciable medullary cavity. Differentials are pyknodysostosis and heavy-metal poisoning. The diagnosis of osteopetrosis can primarily be made by clinical and radiographic features.

Keywords: Bone, Paediatric, Sclerosing dysplasia

CASE REPORT

A 6-year-old Indian female from Vadodara district of Gujarat State, India was referred to the ENT Department of the Baroda Medical College, with history of persistent discharging sinus over nasal bridge. There was history of loss of vision at the age of 2 years and repeated trauma with fractures in both arms and forearms. Patient's birth weight was in the normal range and had normal full term delivery at home with adequate immunization and normal developmental milestones and intelligence. No history of tuberculosis contact. No significant family history. She was the only child of her parents born of non - consanguineous marriage. Written consent was taken from the parents.

Physical examination revealed a very pale child with weight of 17 kg and standing height of 100cm. Head circumference was 45 cm. There was a swelling over the nasal bridge from which foul-smelling pus was draining along with a blood-stained foul-smelling discharge from the right nostril.

INVESTIGATIONS

Blood picture revealed severe anemia (Hb=5 mg/dl), thrombocytopenia (platelets= 95×103/mm^3, normal=165–415×10^3/mm^3), and leucopenia (total WBC=2.9×10^3/mm^3, normal=3.54–9.06×10^3/mm^3). Serum calcium and phosphates were normal, while serum alkaline phosphatase (ALP=219 U/L, normal=33–96 U/L) was raised.

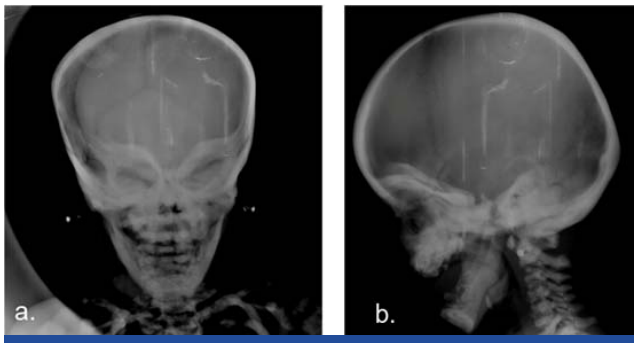
The skull X-ray revealed calvarial and basilar thickening and sclerosis, with poorly developed sinuses and mastoid processes. Mild sclerosis of the nasal bone can be noted [Table/Fig-1a&b]. In chest X-ray, all the ribs and both the clavicles appear sclerotic with homogeneously increased density and no trabeculations or cortico-medullary differentiation [Table/Fig-2a]. X-ray pelvis with both hips shows a curved line paralleling each iliac crest (arrows) giving abone within a bone appearance [Table/Fig-2b]. X-ray DL (dorso-lumbar) spine lateral view shows dense sclerotic bands adjacent to the vertebral end plates with normal mid body, giving the appearance of the "sandwich vertebrae" [Table/Fig-2c]. X-ray both knees shows flaring and elongation of the distal femoral and proximal tibial metaphyses, giving the typical appearance of Erlenmeyer flask type deformity. Uniformly increased density of the bone along with obliteration of medullary cavity can also be noted, thus differentiating it from pynknodysostosis. Multiple alternating dense and radiolucent transverse lines in the metaphyses can also be noted [Table/Fig-3a]. Similar radiographic features can be noted in X-ray right wrist with forearm, which additionally shows old healed fracture of midshaft of right ulna [Table/Fig-3b].

Patient is diagnosed as osteopetrosis based on characteristic clinical and radiological findings. Differential diagnosis are pyknodysostosis and heavy-metal poisoning.

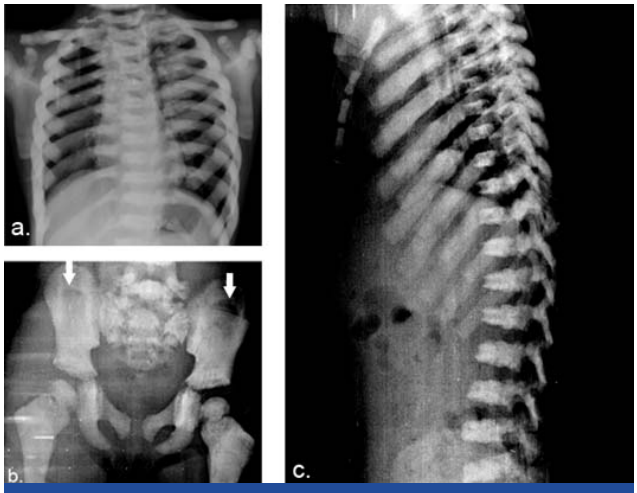
Patient was treated with debridement and saucerization of the sinus, followed by intravenous cefuroxime for 5 days and was discharged on 10th day.

DISCUSSION

Osteopetrosis also known as marble bone disease was described originally in 1904 by Albers-Schonberg [1]. The term "osteopetrosis" was suggested by Karshner in 1926, which is a misnomer, because it literally means "stone-like bone", while the bones are brittle like chalk. The bones appear abnormally



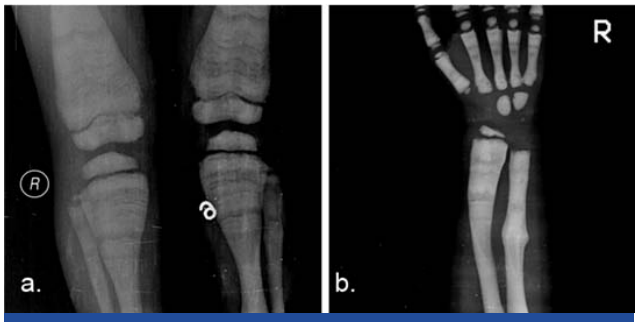
[Table/Fig-1a & b]: X- ray skull AP and lateral views reveal calvarial and basilar thickening and sclerosis, with poorly developed sinuses and mastoid process. Mild sclerosis of the nasal bone can be noted



[Table/Fig-2a-c]: (a) Chest X-ray demonstrates sclerotic ribs and clavicles with homogeneously increased density and no trabeculations or cortico-medullary differentiation (b) X-ray pelvis with both hips reveals a curved line paralleling each iliac crest (arrows) giving a bone within a bone appearance (c) X-ray DL (dorso-lumbar) spine lateral view shows dense sclerotic bands adjacent to the vertebral endplates with normal mid body, giving the appearance of the "sandwich vertebrae"

dense but are actually brittle and are susceptible to frequent pathological fractures [1].

Osteopetrosis is a rare bone disorder characterized by defective osteoclastic resorption of primary spongiosa of the bone result in dense sclerotic bone. Persistence of this primitive tissue, interferes with the formation of mature adult bone with a normal medullary canal, which results in abnormally dense but brittle bones. A balance between osteoblastic bone formation and osteoclastic bone resorption is essential for the normal bone growth which is altered in osteopetrosis. The pathogenesis of osteopetrosis is mediated by abnormal osteoclast function. It can be caused due to interference with the acidification of the osteoclast resorption pit, which may occur due to deficiency of the carbonic anhydrase enzyme



[Table/Fig-3a & b] : (a) X-ray both knees AP view shows flaring and elongation of the distal femoral and proximal tibial metaphyses (Erlenmeyer flask type deformity), with uniformly increased density of the bone along with obliteration of medullary cavity. Multiple alternating dense and radiolucent transverse lines in the metaphyses can also be noted (b) Similar radiographic features can be noted in X-ray right wrist with forearm, which additionally shows old healed fracture of mid shaft of right ulna

encoded by CA2 gene [2]. This enzyme is crucial in proton generation in mature osteoclasts, deficiency of which inhibits the hydrogen ion pumping ultimately resulting in failure to acidify the osteoclast resorption pit [2].

Despite the failure of bone resorption, bone formation continues, resulting in formation of excessive bone. Due to abundance of primitive calcified cartilage, a medullary space is never allowed to form, which leads to anaemia and extramedullary haematopoiesis, causing hepatosplenomegaly. At least 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 recessive type, and (d) a recessive type with renal tubular acidosis (also known as carbonic anhydrase II deficiency syndrome)[3-7]. The severe malignant form may be seen in the child born of consanguineous marriage. A study has classified the various metabolic bone diseases according to the component of the affected bone matrix. Osteopetrosis is included in those caused by low bone remodelling along with pyknodysostosis [8].

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 radiopaque, they are actually brittle and subject to pathological fractures, which are characteristically transverse. Multiple striations producing a bone within a bone appearance may be noted. These are called endobones, which represent fetal vestiges [9]. The skull shows basilar and calvarial thickening with increased density, and poorly developed sinuses. Prognathism may be noted if mandible is involved. Failure of bone remodelling leads to flaring and elongation of the metaphyses of the long bones. There may be vertical or horizontal striations of normal bone interspersed with the

more abundant radio dense primitive tissue, suggesting an intermittent nature of the disease. Vertebrae commonly shows dense bands adjacent to endplates with normal bone in between ("sandwich vertebrae"), however, they may also appear uniformly dense occasionally.

Various bone diseases should be considered in the differential diagnosis of osteopetrosis, particularly pyknodysostosis, and heavy-metal poisoning [10]. Pyknodysostosis can be distinguished from osteopetrosis by lack of anemia and the preservation of the medullary canal. Intoxication of lead, phosphorus, and bismuth may also produce generalized ostesclerosis, however, such cases are usually associated with relevant history.

Clinical features includes severe anemia, repeated bleeding episodes and infections, hepatosplenomegaly, lymphadenopathy, frequent pathological fractures from minor trauma, and failure to thrive. Cranial neuropathies may occur due to encroachment by the bony canal. Commonly affected nerves include optic and vestibule cochlear nerves, resulting in blindness and deafness. Most common causes of death in osteopetrosis include bleeding diathesis and recurrent infections. Laboratory investigations usually reveals varying degrees of anemia, which may be associated with thrombocytopenia. Serum calcium and alkaline phosphatase levels may be elevated. However, the diagnosis of osteopetrosis is primarily based on clinical features and radiographs; a CT scan may be supportive in diagnosis.

Bone marrow transplant is the only durable treatment available for osteopetrosis. Cases of reversal of osteosclerosis have been reported with successful bone marrow transplant [11]. As pathological fractures are quite common in osteopetrosis, it is vital that care is taken to prevent or minimize tendencies for a fracture to occur. It include careful handling of an affected child, "fall-proofing" houses, use of appropriate protective gear like shoes, along with exercise which is safe and do not require too much impact.

CONCLUSION

Osteopetrosis may present clinically as osteomyelitis. Osteopetrosis may cause constriction of the canals containing neurovascular bundles supplying facial bones and jaws, leading to bone necrosis and dental caries, with end result being osteomyelitis. Diagnosis of osteopetrosis can be reached with clinical and radiological findings.

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