Osteopetrosis with Obstructive Hydrocephalus

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Abstract

Osteopetrosis is a congenital disorder characterized by defective osteoclastic resorption of bone that results in brittle bones with increased density. Clinical symptoms include anemia, thrombocytopenia, hepatosplenomegaly, cranial nerve and brainstem compression and hydrocephalus due to foraminal narrowing at skull base. This is a case report of a 6 year old female child who presented with ear discharge since birth, loss of vision at 4 years of age and continuous headache and vertigo for the past 7 months. Radiographs revealed generalized increased bone density, multiple rib fractures and fractures of both the femora. CT brain revealed hydrocephalus for which she underwent shunt surgery 4 months back.

Key Words: Osteoporosis; Bone density; Bone fractures; Hydrocephalus.

Introduction

Osteopetrosis, also known as marble bone disease is caused by osteoclastic dysfunction due to deficiency of carbonic anhydrase enzyme in them. This causes defective hydrogen ion pumping by osteoclasts and this in turn causes defective bone resorption. Hence bone resorption fails while its formation persists resulting in dense yet brittle bones. Due to excessive bone production the marrow space within the bone is markedly reduced, limiting the production of blood cells and leading to pancytopenia. Patients therefore present with recurrent infection, anemia, hepatosplenomegaly (due to extramedullary hematopoiesis) and multiple fractures. It can also cause blindness, facial paralysis and deafness due to nerve compressions by the extra bone formation. Patients can also present with hydrocephalus due to foraminal narrowing at skull base. This case report describes a patient who was diagnosed as a case of osteopetrosis with acquired aqueductal stenosis.

Case Report

A 6 years old female child, delivered through normal vaginal delivery at full-term presented with complaints of bleeding from ear since birth and ear discharge for the past 7 months. The blood from the ear was clotted and the ear bled almost all the time. The discharge was continuous, scanty and foul smelling. Bleeding and discharge were associated with continuous pain and intermittent fever. The complaints were relieved after taking medication and recurred when medication was stopped. There was a history of reduced appetite and increased sleep and also complain of continuous headache and vertigo. She cried immediately after birth and was on mother’s feed for 2 years. Weaning was started at 6 months. Presently her diet includes milk and bananas. There was history of delayed milestones (Neck holding 9 months, sitting 1 year, walking 2 years and she still cannot run). All vaccinations were received according to EPI schedule. On examination she weighed 12 kg and was 86 cm in height. She had a head circumference of 53cm. All muscles showed generalized decrease tone and power. Examination of 2nd, 3rd, 4th and 6th cranial nerves was normal. Radiographs showed generalized dense marble bones. There were multiple rib fractures and fractures of both femora. Lucent transverse metaphyseal bands were visible in long bones which also showed Erlenmeyer Flask Deformities. X-Ray of the skull showed frontal bossing, sclerosis of the mastoid, base of skull and orbital plates. (Figure 1)

Figure 1: X ray skull (lateral view) showing generalized increase in bone density, sclerosis at base of the skull, frontal bossing, widening of sutures and bulge at the anterior fontanelle.
Figure 2: CT Brain showing dilatation of lateral and third ventricles with sparing of fourth ventricle, suggestive of obstruction at the level of aqueduct of Sylvius.

CT Brain revealed dilatation of both lateral and the third ventricles with sparing of the 4th ventricle. It showed sclerosis of the mastoids, base of skull and orbital plates. On the basis of clinical presentation and laboratory and radiological findings, she was diagnosed as a case of osteopetrosis with obstructive hydrocephalous due to acquired aqueductal stenosis. She underwent shunt surgery 4 months back at DHQ Hospital. She also underwent incision and drainage of mastoid abscess 2 months back.

Discussion

Normal bone growth is achieved by a balance between bone formation by osteoblasts and resorption by osteoclasts. In osteopetrosis osteoclast dysfunction mediates the pathogenesis of this disease. There is overgrowth of bone which becomes thick, dense and sclerotic. Their increased size does not improve their strength instead their disordered architecture results in weak and brittle bones which leads to multiple fractures and poor healing.

There are two types of osteopetrosis: the malignant infantile type and the adult type. The adult type is autosomal dominant and is also known as Albers Schonberg disease. It is a milder form which is often asymptomatic and is detected by coincidental radiographic findings of non-traumatic fractures, osteoarthritis of hip, Ruger Jersey spine, sclerosis and osteomyelitis. The infantile type is more severe and presents earlier and hence is referred to as “malignant infantile” type. It is autosomal recessive and the defect lies in chromosome no 11q13. Recently mutation in SNX10 gene has been identified as a cause of autosomal recessive osteopetrosis. Presentation may be at birth, infact some children are still born. Those who survive present with failure to thrive, cranial nerve compressions, fractures, intra cerebral hemorrhages and bone marrow failure.

Visual disturbances are the most common presenting complaints. Failure to achieve normal visual milestones, roving eye movements, squint and blindness are reported resulting from optic nerve compression due to abnormal growth of bones encroaching upon the cranial foramina. Other nerves commonly involved are olfactory, trigeminal, facial and cochlear nerves presenting with hearing loss and facial paralysis.

Patients generally have weak and dense skeleton. Bones are susceptible to fractures with minimal trauma and patients usually have multiple healed fractures. Appearance of bone within a bone and Erlenmeyer Flask deformity and metaphyseal splaying is seen in long bones. Bowing of long bones and scoliosis often leads to deformity and dwarfism. Skull shows frontal bossing and sclerosis of the mastoid, base of the skull and orbital plates. The inner table is often more dense as compared to the outer table. Paranasal sinuses are poorly pneumatized.

Bone marrow space within the bone is markedly reduced owing to excessive bone production and this limits the production of normal blood cells leading to pancytopenia. Patients often present with signs of marrow failure like anemia, recurrent infections, excessive bruising and intracerebral hemorrhages. Erlenmeyer Flask deformity in long bones and hair on end appearance of the skull result from increase hematopoietic activity. Hepatosplenomegaly and lymphadenopathy often result due to compensatory hematopoiesis.

The development of dentition is severely disturbed in children with osteopetrosis. Dental findings include delayed tooth eruption and impaction, aplasia, unerupted and malformed teeth and early tooth loss. Osteomyelitis of the mandible is also a common finding.

Patients with autosomal recessive disease can also present with obstructive hydrocephalus due to foraminal narrowing at skull base where osseus changes are marked. Venus outflow obstruction at cranial foramina along with reduced intracranial space for cerebrospinal fluid to flow around the hemispheres could be a contributing factor. Hydrocephalus can also occur as a result of acquired aqueductal stenosis caused by extensive calcification of tentorium cerebelli and calvarial hyperostosis.

Treatment options for osteopetrosis include: interferon gamma to delay disease progression. Calcitonin (active form of vitamin D) is given to stimulate osteoclasts. Prednisone improves hemoglobin and platelet count. Physical and occupational therapy is suggested to develop motor and other skills. A balanced diet is very essential to support normal growth and development. Orthopedic care is essential for fractures. Monitoring of ear nose and throat and maintaining good dental care is important to decrease the incidence of recurring infections. For obstructive hydrocephalus the treatment is surgical using cerebral...
shunts like ventriculo-peritoneal, ventriculo-atrial and ventriculo-plural. However, excessive bone mass at the skull base can obstruct these shunts and lead to their malfunctions. In such cases endoscopic third ventriculostomy is the treatment of choice. Prognosis is poor for those who have early hematological impairment. Bone marrow transplant is the only choice for survival in such patients. Death usually occurs secondary to bone marrow failure with recurrent infections, massive hemorrhage or transformation to leukemia and its consequences.

References