Aqueductal stenosis with optic atrophy in case of malignant osteopetrosis

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Abstract

Malignant osteopetrosis is a rare autosomal recessive bone disease usually present with short stature, severe anemia, thrombocytopenia, hepatosplenomegaly, and macrocephaly. Here we report a rare case of malignant osteopetrosis presented with evidence of short stature, anemia, thrombocytopenia, hepatosplenomegaly, rickets, aqueductal stenosis, and hydrocephalus with resultant optic atrophy.

Key words: Aqueductal stenosis, malignant osteopetrosis, osteoclasts, rickets

INTRODUCTION

The incidence of malignant osteopetrosis is 1 in 200,000–500,000 population.[1] Malignant osteopetrosis is caused by a defect in osteoclast function. The degradation of mineralized extracellular matrix of bone requires acid secretion by osteoclast membrane. In most of cases disturbances of osteoclast specific subunit of vacuolar proton pump (TCIRG1).[2,3] Defective bone resorption by osteoclasts leads to excessive bone deposition.[3,4]

Usually patient present with parental concern regarding child vision, failure to achieve normal milestones, roving eyeball movements with or without squint, failure to thrive, and recurrent infections. Less commonly associated features are hypocalcemic seizures, excessive bruising, bone fracture, nasal congestion, and abnormal facial appearance.[5]

Here we report a rare case presented with evidence of failure to achieve normal milestones, roving eyeball movements without squint, failure to thrive, recurrent infections, short stature, anemia, thrombocytopenia, hepatosplenomegaly, rickets, aqueductal stenosis, and hydrocephalus with resultant optic atrophy.

Usually cases are diagnosed on X-rays, sometimes bone marrow biopsy required. Molecular diagnosis is also possible.

Bone marrow transplantation is the only effective treatment for osteopetrosis; it provides hematopoiectic stimulus that can differentiate into normal osteoclasts along with supportive treatment related to complications.

CASE REPORT

A 6-month-old male child was first child of third-degree consanguineous marriage born by vertex vaginal delivery with birth weight 2.75 kg presented with intermittent fever and abdominal distension since 1 month, developmentally delayed able to hold neck partially, cooing but not able to recognize mother and transfer objects from one hand to other hand. Anthropometry wise weight was 5.6 kg, length was 60 cm, and head circumference was 44 cm with upper segment/lower segment ratio maintained. On clinical examination, the following were determined: pale, bulging anterior fontanelle 3 × 2 cm with dilated prominent...
veins over scalp, frontoparietal bossing, roving eyeball movements with sunset sign, and hepatosplenomegaly.

Laboratory workup shows anemia with Hb 9.3 gm/dl (after blood transfusion), Hct 27%, reduced platelets, and RBCs on smear with leucocytosis (26,900/mm³). Blood culture shows no growth. Fundus examination reveals bilateral optic atrophy. A radiographic skeletal survey revealed diffuse bony sclerosis and bone in bone appearance involving long bones, spine, and skull, and significant metaphyseal freying and cupping with increased distance between metaphysis and epiphysis s/o osteopetrosis with rickets [Figures 1 and 2]. Magnetic resonance imaging of the brain showed bilateral moderate dilatation of lateral and third ventricle with funneling of proximal portion of aqueduct of sylvius s/o aqueductal stenosis. Aneurysmal dilatation of great cerebral vein of Gallen and straight sinus and significant dilatation of other sinuses. Paucity of white matter in bilateral cerebral hemisphere with thinning of corpus callosum [Figure 3]. CT orbit s/o bilateral optic atrophy left side more than right side.

DISCUSSION

Malignant osteopetrosis is an autosomal recessive disorder common in consanguineous population with 25% risk (i.e., 1 in 4) of having another child affected in subsequent pregnancy. It is a serious lethal disorder that leads to death in infancy and childhood. The age at diagnosis was 3–18 months, and mean life expectancy without bone marrow transplant was 3.7 years.[3]

Most of the manifestations are due to failure to remodel growing bones. This leads to narrowing of cranial foramina and encroachment on marrow spaces resulting in optic nerve, facial nerve dysfunction, and anemia accompanied by compensatory extramedulary hematopoiesis in liver and spleen results as hepatosplenomegaly, leucopenia, and thrombocytopenia.[2,6]

Our case presented with evidence of failure to achieve normal milestones, roving eyeball movements without squint, failure to thrive, recurrent infections, short stature, rickets, anemia, thrombocytopenia, hepatosplenomegaly, aqueductal stenosis, and hydrocephalus with resultant optic atrophy.

Rickets is a paradoxical complication in osteopetrotic bones due to inability of osteoclasts to maintain calcium and phosphate balance in extracellular fluid.[4] Recurrent infections are due to defect in generation of superoxide by leucocytes along with anemia, poor nutrition and recurrent hospitalization.[5] Another unusual complication associated

Figure 1: X-ray showing thickening of skull bones, bone in bone appearance involving all bones with freying and cupping at the ends of long bones

Figure 2: X-ray showing osteopetrosis with rickets

Figure 3: MRI brain showing paucity of white matter with thinning of corpus callosum, moderate dilatation of lateral and third ventricles with aqueductal stenosis
with osteopetrosis is aqueductal stenosis with progressive hydrocephalus. In our case there was a progressive blindness due to optic nerve compromise, possibly from increased intracranial pressure as a consequence of hydrocephalus and venous outflow obstruction at the constricted skull base, in addition to direct compression within the optic canal.

Management of osteopetrosis is multidimensional involving pediatrician, ophthalmologist, orthopedician, otorhinologist, physiotherapist, and so on. Human leukocyte antigen-matched bone marrow transplant is the treatment of choice. Treatment of rickets with calcitriol (1,25-hydroxyvitamin D₃) and high levels of dietary calcium decrease the prevalence of lethargy, irritability, poor feeding, and upper respiratory tract infection in these patients[^2][^4].

Our patient treated with antibiotics for infection, vitamin D, and calcium supplement given and bone marrow transplant is planned.

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