Case Report

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A Case Report of Hyperphosphatasia Treated with Pamidronate

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ABSTRACT

Background: Hereditary hyperphosphatasia is a congenital and rare disease with high bone turn over. The disease is defined with extremely elevated alkaline phosphatase levels. Neonates with hyperphosphatasia are normal at birth but develop progressive long bone deformities, fracture, vertebral collapse, skull enlargement due to massively thickened calvarium, and deafness.

Case Presentation: Here, we described a male patient with progressive deformity in limbs and pain during walking that onset of symptoms was from age of two. The patient admitted to the Shahid Sadoughi Hospital, Yazd, was born from a non-consanguineous marriage. He was treated with pamidronate until halt of the disease progression and followed up for 18 months.

Conclusion: Bisphosphonate is the treatment of choice for hyperphosphatasia because it can normalize bone turnover, improve growth rates, and skeletal quality.

Introduction

Hereditary hyperphosphatasia is a rare high bone turn over and autosomal recessive bone disease with extremely elevated alkaline phosphatase levels and normal calcium and phosphate levels which occurs in infancy or early childhood with male predilection.[1,2] Families have been characterized as having a homozygous deletion of the *TNFRSF11B* gene that encodes osteoprotegerin (OPG).[3] The loss of OPG function results in generalized extremely rapid bone turnover.[4] Bone turnover is high and its markers such as alkaline phosphatase and hydroxyproline are increased.[5]

The phenotypic variability ranges from presentation in infancy with severe progressive deformity to presentation in late childhood with minimal deformity.[6] Osteoid proliferation in the subperiosteal portion of

bone leads to separation of the periosteum from the bone cortex. Bowing and thickening of the diaphysis are common along with osteopenia. Affected children are normal at birth but the disease usually has its onset by 2-3 years of age when painful deformity developing in the extremities results in abnormal gait and sometimes fractures. Other common findings include pectus excavatum, kyphoscoliosis, and rib fraying. The skull is long and the cranium is thickened and may be deformed. Progressive and profound hearing loss can arise because of skull involvement.[7]

On radiographs, the bony texture is variable, dense area interspersed with radiolucent areas and general demineralization (cotton- wool appearance). Long bones appear cylindrical, lose metaphyseal modeling, and contain pseudocysts that show a dense, bony halo.[7]

At present, treatment is far from optimal and consists of calcitonin to reduce bone turn over and bisphosphonates to inhibit bone resorption. Therapy with recombinant osteoprotegerin has shown promising results in adults.[6] Intravenous pamidronate therapy can reduce the rapid bone turnover, bone pain, prevent deformity and disability and improve hearing. However, this effect can be transient. In case of resistance to pamidronate therapy, switching to another bisphosphonate like zoledronate may provide long-term clinical and biochemical improvement as an alternative treatment.[5] Cyclical intravenous pamidronate (1 mg/kg/day during 3 h, 3 consecutive days at 2- to 3-month intervals) administration for 2 years with oral calcium 500 mg and vitamin D 1000 IU/day and oral pamidronate addition after 11 months of intravenous therapy (I .V. therapy) is also effective.[8]

Case Presentation

A 5-year-old boy presented to the clinic with progressive deformity in limbs (Figure 1, 2, 3) and pain during walking from the age of 2. He had also increased head circumference and a history of left humerus bone fracture at birth. The parents had no consanguinity.

Figure 1. Bowing of legs

In his physical examination, growth index was as below:

Weight: 16 kg (10%), Height: 109 cm (50%) and Head circumference: 53 cm

Laboratory tests were as below:

calcium: 10.6 mg/dl (NL:8.5–10.5)

phosphate: 5.3 mg/dl (NL:3.5–6.6)

alkaline phosphatase: 8211 U/L (NL:133-347)

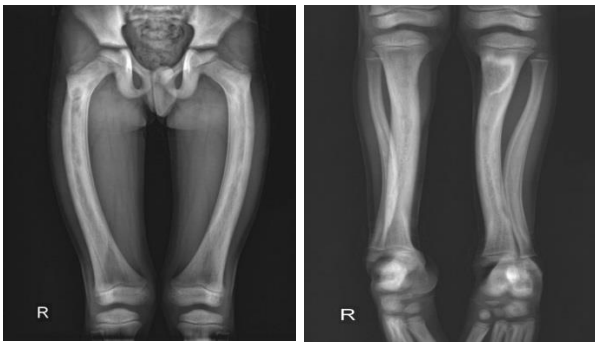

Figure 2. Bowing and thickening of the diaphysis and osteopenia

Radiographs showed large skull and thickened cranium with cotton wool appearance (Figure 4).

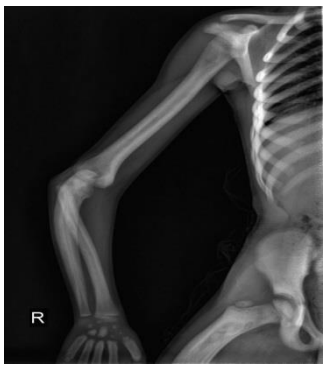

Figure 3. Deformity of ulna and radial bones is seen

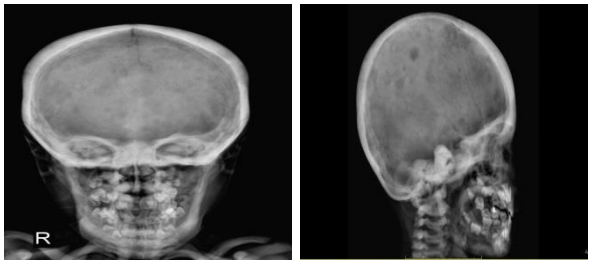

Figure 4. Skull is large and cranium is thickened with the cotton wool appearance

With the diagnosis of hyperphosphatasia, cyclical intravenous pamidronate (1 mg/kg/day during3 h, 3 consecutive days at 3-month intervals) started for him for 3.5 years. During treatment, limb deformities do not progress and he is good after 18 months follow up.

Discussion

We report a 5- year- old boy with progressive deformity of limbs and pain during walking from 2 years ago. With the diagnosis of hyperphosphatasia, he was treated with cyclical intravenous pamidronate (1mg/kg/day during 3 consecutive days at 3-month intervals for 3.5 years).

During treatment and 18 months follow up, limb deformity has shown no progress and bone pain has been resolved.

In similar studies, bisphonate (pamidronate) is selective treatment for improving growth rates and skeletal quality.[8]

Treatment with pamidronate is not a definitive treatment and due to the rarity of the disease, the authors of present article are interested in using the experiences of researchers.

Conclusion

Hereditary hyperphosphatasia is a rare autosomal recessive disorder (prevalence < 1 in 10 million). Its progressive skeletal deformities are associated with multiple fractures, which become apparent in the second or third year of life and result in dwarfing and sporadic cranial nerve involvement; loss of normal cortical outlines with the involvement of long bones from epiphysis to epiphysis. Serum calcium and phosphate levels are normal. The diagnosis establishes based on clinical, radiological, and histological features. Fractures, deformities, diffuse sclerosis on radiographs and high serum alkaline phosphatase is characteristic. As bisphosphonate can normalize bone turnover, improve growth rates, and skeletal quality, it is the treatment of choice for hyperphosphatasia.

Conflict of Interests

Authors have no conflict of interests.

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