OSTEOGENESIS IMPERFECTA FOUNDATION

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The Osteogenesis Imperfecta Foundation, Inc. is the only voluntary national health organization dedicated to helping people cope with the problems associated with osteogenesis imperfecta. The Foundation's mission is to improve the quality of life for people affected by OI through research to find treatments and a cure, education, awareness, and mutual support.

OI Issues: Hypophosphatasia

Definition

Hypophosphatasia is one of several disorders that resembles osteogenesis imperfecta. It is an inherited metabolic (chemical) bone disease that results from low levels of an enzyme called alkaline phosphatase (ALP). Enzymes are proteins that break down other chemicals in the body so the body can use them. ALP is normally present in large amounts in bones and the liver. In hypophosphatasia, abnormalities in the gene that makes ALP lead to the production of inactive ALP. Subsequently, several chemicals, including phosphoethanolamine, pyridoxal 5′-phosphate (a form of vitamin B_6) and inorganic pyrophosphate, accumulate in the body and are found in large amounts in the blood and urine. It appears that the accumulation of inorganic pyrophosphate, an inhibitor of mineralization, is the cause of the characteristic defective calcification of bones seen in infants and children (rickets) and in adults (osteomalacia).

The severity of hypophosphatasia is remarkably variable from patient to patient. The most severely affected fail to form a skeleton in the womb and are stillborn. The mildly affected patients may show only low levels of ALP in the blood, yet never suffer bone problems.

In general, patients are classified as having "perinatal," infantile," "childhood," or "adult" hypophosphatasia depending on the severity of the disease and the age at which the bony manifestations are first detected.

Odontohypophosphatasia refers to children and adults who have only dental, not skeletal, problems. This usually involves premature loss of teeth.

The x-ray changes are quite distinct to the trained eye, and the diagnosis is substantiated by measuring ALP in a routine blood test. It is important that the doctors use appropriate age ranges for normal ALP levels when interpreting the blood test. Gene testing for hypophosphatasia is now available.

Prevalence

It has been estimated that the severe forms of hypophosphatasia occur in approximately one per 100,000 live births. The more mild childhood and adult forms are probably somewhat more common. About one out of every 300 individuals in the United States is thought to be a carrier for hypophosphatasia.

Symptoms

There are reports of blue sclera (whites of the eyes) during infancy and childhood that may resemble osteogenesis imperfecta. Depending on the severity of the skeletal disease, there may be deformity of the arms, legs and chest. Frequent bouts of pneumonia can result if the chest distortion is severe. Recurrent fractures can also occur, but are not as common as in OI. Teeth may be lost prematurely and the teeth may have wide pulp chambers that predispose them to cavities. These symptoms resemble some of those found in osteogenesis imperfecta.

Prognosis

The outcome following a diagnosis of hypophosphatasia is variable. Cases with severe deformities at birth requiring a ventilator to breathe almost invariably result in death within days or weeks. Long-term survival is very rare. When the diagnosis is made not at birth, but before six months of age, some babies have a downhill course, while others spontaneously improve and do well. When diagnosed during childhood, underlying rickets may or may not result in the presence of skeletal deformities. Premature loss of teeth (when the child is under the age of five) is the most usual manifestation. Adults may be troubled by recurring fractures in their feet and painful, partial fractures in their thigh bones.

Treatment

There is no established medical therapy for hypophosphatasia. Forms of bone marrow transplantation have seemed beneficial for two babies with the infantile form. One adult appeared to benefit from injections of a form of parathyroid hormone. Bone rodding can be helpful for persisting fractures.

Inheritance Factors

The severe perinatal and infantile forms of hypophosphatasia are inherited as autosomal recessive conditions. The patient receives one defective gene from each parent. Some of the more mild childhood and adult cases are also inherited this way. Some mild adult cases are inherited in an autosomal dominant pattern where the patient gets just one defective gene from one parent. Here, hypophosphatasia can affect several generations.

Individuals with hypophosphatasia and parents of children with this disorder are encouraged to seek genetic counseling to understand the likelihood and severity of hypophosphatasia recurring in their family.

For more information about osteogenesis imperfecta contact:

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