

An Infantile Hypophosphatasia Patient with a Homozygous Mutation in the *ALPS* Gene

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Hypophosphatasia is an autosomal recessive and less frequently autosomal dominant hereditary congenital bone disease. It is marked by a deficiency of alkaline phosphatase (ALP) activity in the liver, bones, and kidneys and is associated with defective skeletal mineralization. It has been estimated that severe forms of hypophosphatasia occur in approximately in 1/100 000 live births. Four forms of hypophosphatasia have been identified depending on the age of manifestation; perinatal (lethal), infantile, childhood, and adulthood. Odontohypophosphatasia characterized by dental findings and pseudohypophosphatasia characterized by normal serum ALP levels are also present. It is caused by loss-of-function mutations in the tissue nonspecific *ALP* gene (*TNSALP*), the gene encoding the isoenzyme TNSALP, which is located in the chromosome region 1p36.1–1p34 [1]. The clinical severity is associated with the age of diagnosis and the lack of TNSALP activity. The mortality rate is around 50% in perinatal and infantile forms due to respiratory failure and pneumonia. Hypercalcemia and hypercalciuria due to defective skeletal mineralization

are seen in severe early-onset form. Radiological findings may be similar to rickets. It can be distinguished from rickets by low ALP levels. Radiography shows widespread demineralization and rachitic changes in the metaphyses of long bones. Calcitonin therapy was used in infantile form but is not a definitive treatment. Recently, there has been a research on enzyme-replacement therapy and bone marrow transplantation. We presented an infantile hypophosphatasia patient with a homozygous mutation in the *ALPS* gene.

Case: A 1.5-month-old male patient was evaluated because of short limbs and epilepsy. He was the first male child born alive from the first pregnancy at term by cesarean section. There was no consanguinity between the parents. Physical examination revealed a flattened facial appearance, broad forehead, flattened nasal bridge, low-set ears, short neck, narrow thorax, shortening of the left arm, and dimples on knees. Laboratory tests revealed hypercalcemia, hypercalciuria, and low ALP. Metaphyseal irregularities, cupping, and diaphyseal shortening in bone radiographs were detected. A homozygous mutation was detected in the operated *ALPS* gene.

Discussion: In patients with rickets, if hypercalcemia and ALP impairment are determined, the rare disease hypophosphatasia should be kept in mind. Although enzyme-replacement therapy may appear to be a treatment in the future, still there is no current therapy. In these patients, early diagnosis is important for clinical follow-up, genetic counseling, and prenatal diagnosis.

Key words: Hypophosphatasia, infantile type, hypercalcemia, alkaline phosphatase, *ALPS* gene