

SHORT COMMUNICATION

HYPOPHOSPHATASIA: A SERIES OF DIAGNOSIS MISSTEPS

Madson KL¹, Mack KE¹, Zika S¹, Whyte MP^{1,2}

Corresponding Author Katherine L. Madson PhD/MD, Contact Information: Center for Metabolic Bone Disease and Molecular Research, Shriners Hospital for Children 2001 S Lindbergh Blvd, St Louis, MO 63131, USA

¹Center for Metabolic Bone Disease and Molecular Research, Shriners Hospital for Children, St Louis, MO, USA ²Division of Bone and Mineral Diseases, Washington University of Medicine at Barnes-Jewish Hospital, St Louis, MO, USA E-mail address to corresponding author: kmadson@shrinenet.org

We report a 3-½-year-old boy whose hypophosphatasia (HPP) diagnosis was delayed elsewhere by two years through a series of errors interpreting clinical, laboratory, and radiographic characteristics of this inborn-error-of-metabolism.

He was of German-Mexican heritage living in California and developed bowing of legs at 12 months-of-age following weight bearing at 11 months-of-age. His pediatrician diagnosed “physiologic bowing”. At age 17 months, he had non-traumatic loss of a central mandibular incisor with root intact. The community pediatric dentist told the parents that this was an abnormal situation, but the tooth could not be re-attached. At age 18 months, a 2nd tooth was lost without trauma; the parents were told that if he lost any additional teeth, “he should be entered into a research study”; the pediatrician’s note says the dentist mentioned acid phosphatase deficiency as an etiology.

Mother began to search the internet using the keywords “bowing and tooth loss” and found HPP. She presented this information to the pediatrician and requested testing for HPP with laboratory evaluation and referral of her child to an orthopedist for the bowing. The orthopedist’s x-rays were “normal” for a 20-month old, and we agree that the films

“did not suggest Blount’s Disease” (tibia vara). Four months later, knee radiographs showed “metaphyseal spurs”, now diagnosed elsewhere as Blount’s Disease (but revealing rachitic changes), and he was treated with hi-knee- ankle-foot orthotics.

During the pediatrician’s laboratory evaluation for HPP, acid phosphatase was ordered by the clerks on two separate occasions. A serum alkaline phosphatase level of 90 u/L on the metabolic panel reviewed during referral to a pediatric geneticist was judged “normal” using an adult normative range (50 - 136 u/L). The age-appropriate pediatric range was not provided. Similarly, other HPP substrate tests at that time were ordered by the clerks as Vitamin B1, rather than Vitamin B6 (pyridoxal 5’-phosphate), and as phosphotidylethanolamine auto-antibodies IgG, IgA, IgM, rather than phosphoethanolamine. The diagnosis of HPP by the geneticist was finally made at Connective Tissue Gene Tests (Allentown, PA) when a heterozygous mutation on exon 10 c.1034C>T with amino acid Ala345Val was found.

Typically, the diagnosis of HPP can be made from the disorder’s clinical, laboratory, and radiographic characteristics.