

“My bones hurt” – A rare case of unrecognized Familial Hypophosphatasia treated with Asfotase Alpha

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Introduction

Hypophosphatasia (HPP) is the inborn error of metabolism that features low serum alkaline phosphatase (ALP) activity (hypophosphatasemia) caused by loss of function mutation of the gene that encodes the tissue- nonspecific isoenzyme of ALP. It was first described in 1948 in Canada by John C. Rathbun after an infant patient died after presenting at 2 months of age with rickets and seizures yet had paradoxically low alkaline phosphatase activity in the serum and bone and other tissues obtained on autopsy. The incidence of HPP varies approximately 1 in 2500 to 1 in 300,000 depending on severity; more prevalent in Caucasian than in Black people in the United states. It may be inherited as either an autosomal recessive or autosomal dominant trait. There are six major clinical forms of HPP varying in severity and age of presentation- prenatal, perinatal, infantile, childhood, adult, odonto-hypophosphatasia. Asfotase alpha is the first approved medical treatment for perinatal, infantile, and juvenile onset HPP. Here we present a case of childhood hypophosphatasia, undiagnosed until adulthood, and later treated with asfotase alpha.

Conclusion

Hypophosphatasia is a rare condition. There are currently no FDA approved treatments for hypophosphatasia in adults. Some reports of treatment with teriparatide and with monoclonal anti-sclerostin antibody have been published. It is essential to think about this as a potential diagnosis when an adult patient presents with multiple stress fractures. This condition can have a varied presentation even when it occurs in the members of the same family. This patient was diagnosed much later in adulthood and was treated with Asfotase alpha with good response.

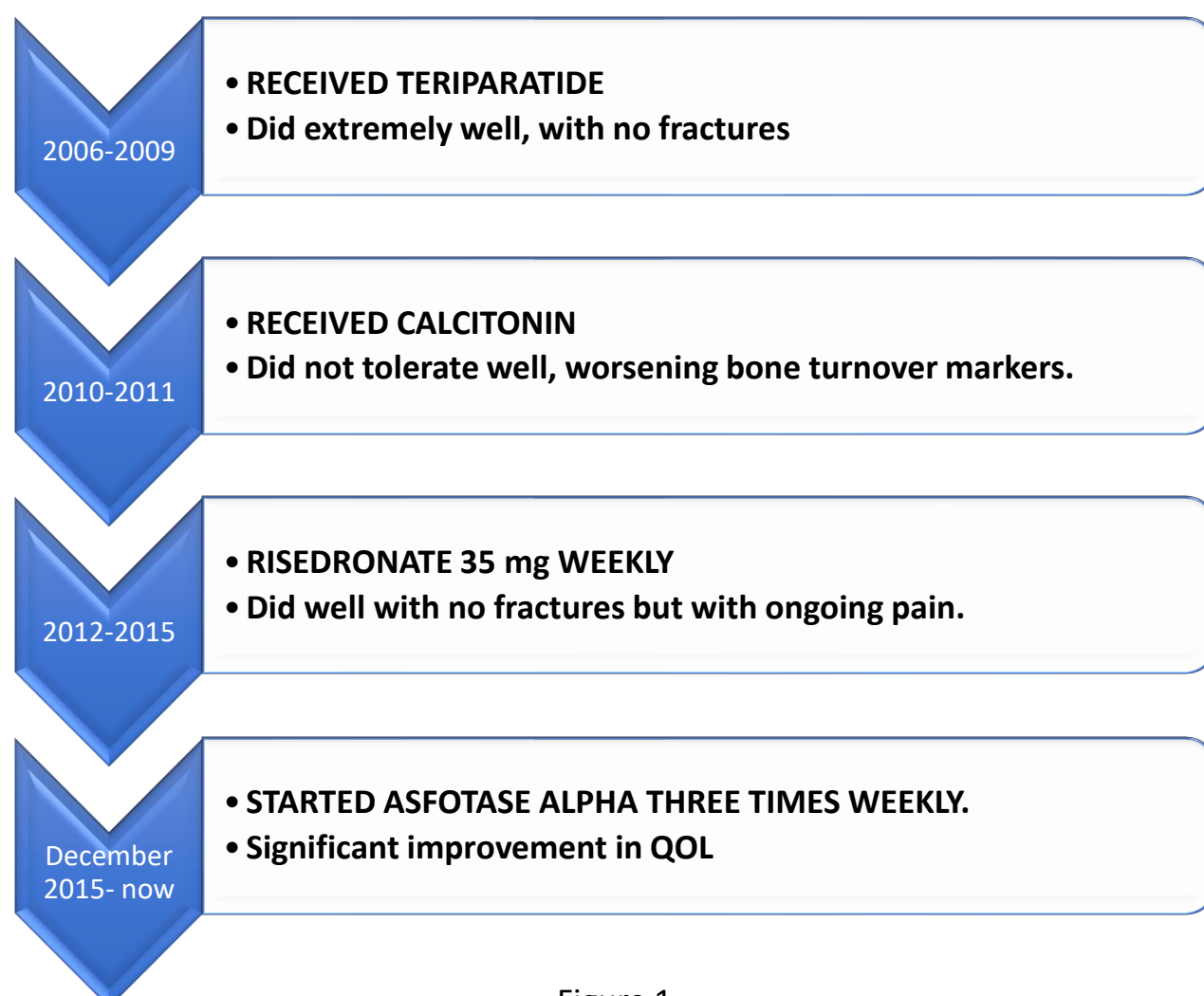


Figure 1

Case Presentation

A fifty-three-year-old female with a past medical history of seizure disorder, hearing loss and osteoporosis presented to the endocrinology clinic for evaluation of multiple stress fractures. She also reported gum disease with gradual loss of teeth at age 16, seizures through age 40, problems with walking due to pain in the bilateral thighs at age 47 with eventual development of bilateral atypical fractures with rods placed in both femurs. She was first diagnosed with osteoporosis and treated with anti-resorptive therapy for about one and half year prior to office visit. She had a family history of osteoporosis in her mother, diabetes and osteoporosis in her father, Paget’s disease in a paternal aunt, but no known bone disease in her siblings or children. On physical exam she was noted to have missing teeth, hearing loss more prominent in the right, scars in her extremities from prior surgeries, her left lower extremity was relatively shorter than her right lower extremity. Her spine exam was unremarkable with no kyphosis and heart and lung exam were unremarkable.

On laboratory evaluation she was noted to have normal electrolytes, kidney function, normal total calcium, normal ionized calcium and normal PTH. Her vitamin D level and Cross linked N-telopeptide was also within normal limit. Her alkaline phosphatase was low at 20 u/l(ref range- 40-150U/L) , and vitamin B6 level was elevated at > 30,400 nmol/L (normal range- 18-175) Her bone densitometry prior to presentation T scores of -3.2 for total hip and -1.3 in spine and Z score of -2.3 in hip and -0.1 in spine. Since her initial presentation, her treatment regimen have been outlines in figure 1.

In 2015, she was started on Asfotase alpha 2mg/kg three time weekly. Following that the patient reported significant improvement in bone pain, was now able to cut up her meat, apply makeup and has more energy. She reports significant improvement in her quality of life and ability to perform activities of daily living independently. On laboratory evaluation, there was significant increase in her alkaline phosphatase level and decrease in Vitamin B6 plasma level (Figure 2).

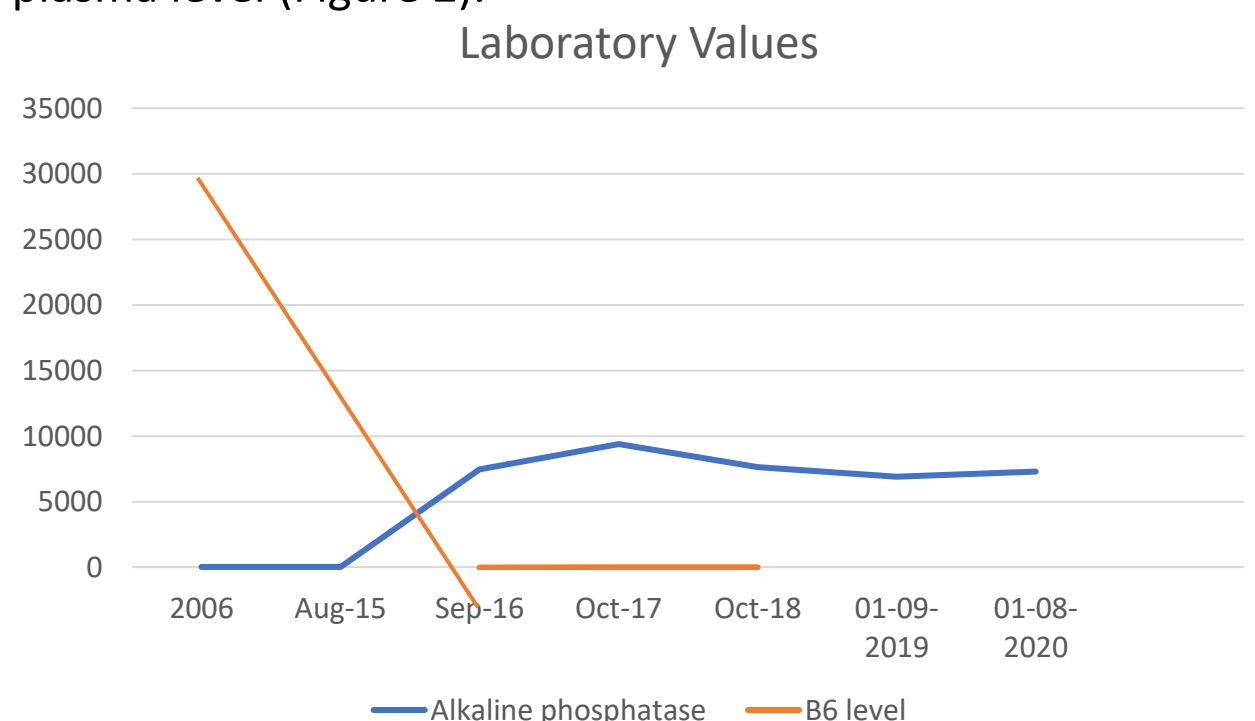


Figure 2

References:

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- Shapiro JR, Lewiecki EM. Hypophosphatasia in Adults: Clinical Assessment and Treatment Considerations. *J Bone Miner Res*. 2017;32(10):1977-1980. doi:10.1002/jbmr.3226