Adult-Onset Hypophosphatasia: Before and After Treatment with Asfotase Alfa

Angela Magdaleno DO
Lehigh Valley Health Network, angela.magdaleno@lvhn.org

Sonum Singh MD
Lehigh Valley Health Network, Sonum.Singh@lvhn.org

Sandhya Venkataraman DO
Lehigh Valley Health Network, Sandhya.Venkataraman@lvhn.org

Ya-Yu Lee MD
Lehigh Valley Health Network, Ya-Yu.Lee@lvhn.org

Published In/Presented At

Magdaleno, A. Singh, S. Venkataraman, S. Lee, Y-Y. (2019, March 25). *Adult-Onset Hypophosphatasia: Before and After Treatment with Asfotase Alfa.* Poster Presented at: The Endocrine Society Conference, New Orleans, LA.

Adult-Onset Hypophosphatasia: Before and After Treatment with Asfotase Alfa

Angela Magdaleno, DO,[1] Sonum Singh, MD,[1] Sandhya Venkataraman, DO[2] and Ya-Yu Lee, MD[1]

[1]Department of Internal Medicine, Division of Endocrinology, Lehigh Valley Health Network, Allentown, PA, [2]Department of Internal Medicine, Lehigh Valley Health Network, Allentown, PA

INTRODUCTION

- Hypophosphatasia is a rare inherited bone disease resulting from mutations in the gene encoding tissue-nonspecific alkaline phosphatase (TNSALP), an enzyme predominant in skeleton, liver, kidney and teeth.
- Diminished TNSALP activity causes accumulation of substrates that inhibit bone mineralization resulting in debilitating pain, fractures and low alkaline phosphatase (ALP) levels.
- In 2015 the FDA approved asfotase alfa, a bone-targeted recombinant TNSALP, for treatment of infant/child onset hypophosphatasia.
- We present a case of hypophosphatasia treated with asfotase alfa resulting in improvements in whole body scan and pedometer step counts.

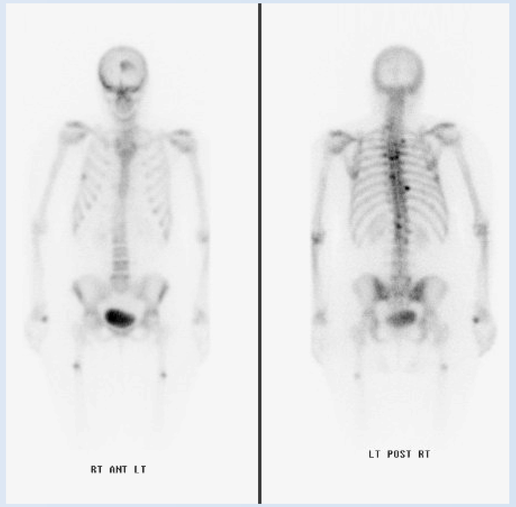
CASE REPORT

- In 2014, a 52-year-old female with chronic pain presented with over 30 years of bony pain, poor balance, falls, fractures and life-long dental disease.
- Physical exam displayed tenderness of long bones and waddling gait.
- Blood work was remarkable for low ALP and low bone-specific ALP. Vitamin B6 level was significantly elevated. Calcium level was normal. Serum phosphorus was elevated. Intact parathyroid hormone level was elevated, with known diagnosis of chronic kidney disease, GFR 27 mL/min. Her 24-hour urine calcium, serum protein electrophoresis, celiac test, thyroid studies and vitamin D level were normal. N-telopeptide was elevated.
- SPECT whole body scan demonstrated increased uptake with multiple fractures of the axial skeleton and proximal femurs; consistent with oncogenic osteomalacia.
- Fibroblast growth factor 23 and indium 111 octreotide scan showed no evidence of malignancy.
- DEXA scan showed osteopenia of the hip and forearm.
- She was diagnosed with hypophosphatasia.
- Initially, due to lack of options, she was treated with denosumab. After three injections, she developed a new atypical femur fracture requiring surgical rod placement; denosumab was discontinued.
- In 2017, she was started on asfotase alfa with significant improvements in balance, endurance, and bone pain.
- Prior to treatment, the patient required narcotic oral pain medicine, fentanyl patch and an assistive device to walk 3000 steps daily; after treatment, she is walking over 10,000 steps daily without any pain pharmacotherapy.
- Repeat whole body scan showed less focal uptake overall, consistent with healing fractures.

TABLE 1.

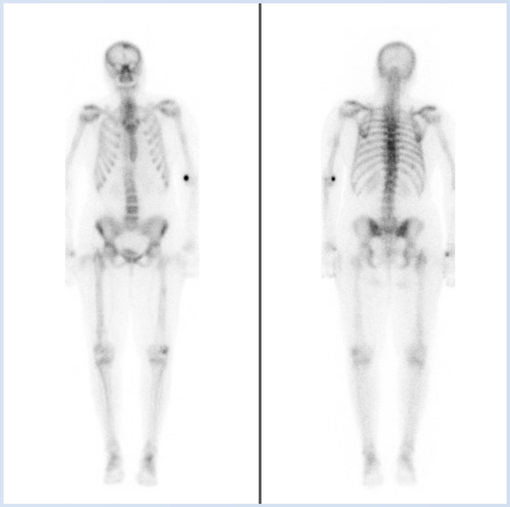
Test	Result	Normal Value
Alkaline Phosphatase	11 U/L	35-120 U/L
Bone-Specific Alkaline Phosphatase	3 ug/L	7.0-22.4 ug/L
Vitamin B6	>2000 nmol/L	20.0-125.0 nmol/L
Calcium	9.8 mg/dL	8.5-10.1 mg/dL
Phosphorus	5.2 mg/dL	2.3-4.6 mg/dL
Intact Parathyroid Hormone	114.1 pg/mL	18.5-88.0 pg/mL
Parathyroid Hormone Related Peptide	3.4 pmol/L	0.0-3.4 pmol/L
Thyroid stimulating hormone	1.83 uIU/mL	0.35-4.00 uIL/mL
25-OH Vitamin D	42 ng/mL	30-100 ng/mL
N-Telopeptide	25.9 nM	6.2 to 19.0 nM

2014 WHOLE BODY BONE SCAN



IMPRESSION:
Extra-axial hyperdense lesion in left frontal region of the calvarium. Multiple fractures and focal areas of increased uptake in the axial skeleton as well as fractures of the proximal third of both femurs.

2017 WHOLE BODY BONE SCAN



IMPRESSION:
Minimal to mild focal activity at posterior right 10th and 11th rib, proximal left femur, vertex of skull, and right femur.

CONCLUSION

- This case highlights clinical proof of improvement after treatment with asfotase alfa based on increased daily step count and healing fractures on whole body scans.
- Asfotase alfa is a newly approved therapy for hypophosphatasia and therefore long-term outcomes are not yet available, however short term patient reported subjective findings and clinical data are reassuring for successful treatment.

LVHN.org

Lehigh Valley Health Network