

Oral Abstract

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Teriparatide-induced alkaline phosphatase and osteoblast activity in an adult with hypophosphatasia

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Hypophosphatasia is a rare genetic disorder characterized by low serum alkaline phosphatase (ALP) and defective bone mineralization predisposing to poorly healing pseudofractures and fractures.¹ Experience with teriparatide in hypophosphatasia is limited.^{2,3}

Aim: To describe the first known bone biopsy proven osteoblast response to teriparatide in an adult with hypophosphatasia.

Methods: A 53-year-old woman was diagnosed with hypophosphatasia on the basis of repeatedly low serum ALP (6-8 IU/L), high urine phosphoethanolamine (52 µmol/mmol creatinine; normal, 5-18) and pseudofractures on the lateral aspect of both proximal femurs. She underwent orthopedic surgery after sustaining a minimal-trauma fracture of the left femur. Teriparatide 20 µg daily was initiated in December for painful non-healing fracture.

Results: The patient reported reduced pain. Serum ALP more than doubled and phosphate levels decreased. Bone formation marker N-terminal propeptide of type I procollagen (PINP) markedly increased. Bone biopsy before and 4 months post-teriparatide revealed increases in osteoblast numbers and activity. However, presently, defective bone mineralization persisted; hence, no callus was apparent on follow-up radiographs.

| | Normal Range | 11/07 | 01/08 | 02/08 | 03/08 | 04/08 |
|----------------------------|----------------|-------|-------|-------|-------|-------|
| Corrected Calcium | 2.1-2.6 mmol/L | 2.33 | 2.48 | 2.51 | 2.49 | 2.49 |
| Phosphate | 0.8-1.5 mmol/L | 1.72 | | | 1.84 | 1.66 |
| ALP | 30-120 IU/L | 8 | 13 | 14 | | 19 |
| PINP | <76 µg/L | 99.1 | | 272 | 286 | 265 |
| Urine N-Telopeptide | 18-38 U | | | | 223 | 173 |

Conclusion: Teriparatide-induced increases in ALP, PINP, osteoblast number and activity together with the decrease in serum phosphate suggest a beneficial effect on bone through stimulation of ALP and osteoblast activity. Longer therapy duration is needed to show effects on fracture healing.

¹ Whyte MP. Hypophosphatasia and the role of alkaline phosphatase in skeletal mineralization. *Endocr Rev.* 1994; 15(4): 439-61.