OSTEOPROTEGERIN/RANKL SYSTEM AND BONE TURNOVER MARKERS IN ONCOGENIC HYPOPHOSPHATEMIC OSTEOMALACIA

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Oncogenic hypophosphatemic osteomalacia (OHO) is a rare paraneoplastic syndrome characterised by elevated fibroblast growth factor 23 (FGF-23) serum levels, hypophosphataemia, urinary phosphate wasting and deranged skeletal metabolism. Characteristically, 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D concentration are also generally overtly low or inappropriately normal relative to the prevailing hypophosphataemia.

Aims of this study were to evaluate serum levels of components of osteoprotegerin (OPG) system and their relationship with bone mineral density and bone turnover markers (bone specific alkaline phosphatase, cross-linked C-telopeptide of collagen type 1 and urinary hydroxyproline/creatinine ratio) in five patients with OHO (M:F 3:2; mean age 56.6±3.7 years). The "reference values" of evaluated parameters were determined in 40 age- and sex- matched healthy control subjects.

OHO patients showed serum levels of ligand of receptor activator of nuclear factor (NF)-κB (RANKL) significantly lower compared to healthy controls (0.52±0.19 vs 1.05±0.23 pmol/L, p 0.024). Bone alkaline phosphatase serum levels in OHO patients were also significantly higher compared to controls (42.8±17.5 vs 17.5±6.7 μg/L, p<0.001). FGF23 serum levels in OHO patients were directly related to L2-L4 BMD (r=-0.724, p<0.014). Levels of OPG and other bone turnover markers were not different between study groups. One year after the complete surgical excision of neoplastic lesions causing OHO in two patients, the reported parameters were within the normal range.

Study results suggest that bone loss during OHO is not related to biological properties of RANKL/OPG system, but could be caused directly by FGF23. In this contest, the functional inhibition of RANKL/OPG system and the increased bone specific alkaline phosphatase serum levels could be considered a compensatory mechanism to bone loss.