Low Level of Alkaline Phosphatase as a Clue to Noncompliance in Patient with Hypophosphatasia

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Introduction: Hypophosphatasia is rare, inherited metabolic disorder caused by mutations in the tissue nonspecific alkaline phosphatase gene. This mutation leads to persistently low level of alkaline phosphatase (ALP) which is the hallmark of the hypophosphatasia but also elevated substrates mostly inorganic pyrophosphate (PPi) and pyridoxal-5-phosphate (PLP). Enzyme replacement therapy (ERT) with asfotase alpha presents currently available medical treatment, in which administration of enzyme leads to increase in ALP activity up to several thousand units per liter. Measurement of ALP and other biochemical parameters are crucial during follow-up of treatment with ERT. Clinical case: 42-year-old female with medical history significant for early onset scoliosis secondary to hypophosphatasia diagnosed at age of 6 months presented at endocrinology clinic to establish care. In early childhood patient had 3 nontraumatic femur fractures and ankle fracture at age 25. Patient underwent fixation of bilateral proximal femurs and spinal surgery due to scoliosis. She has been started on weight base treatment with asfotase alpha 6 years ago with 2 mg/kg 3 times per week. During current visit patient continued to experience back pain despite surgery treatment and ongoing treatment with asfotase alpha. Her ALP level in blood was 234 u/l. This ALP level was low considering that patient is on 6 years long treatment and...
careful history taking revealed that patient is taking smaller dosage of asfotase alpha than recommended. Patient explained that due to side effects of medications: palpitations and nervousness she decreased her dose to 2 times per week which led to inappropriate self-medication and non-compliance. **Conclusion:** Although there are many different causes of low level of ALP like osteogenesis imperfecta, vitamin D intoxication, multiple myeloma, vitamin C deficiency, hypothyroidism, Cushing’s syndrome and bisphosphonate therapy recent studies found out that prevalence of mild form of hypophosphatasia can be much higher than expected even 1/508. Due to relative rarity of the disease and lack of the awareness of hypophosphatasia among physicians there are usually delay in the diagnosis and management especially in mild forms. Measurement of ALP activity is crucial for diagnosis of hypophosphatasia but is also essential minimum for monitoring of treatment. Relatively low level of ALP while on treatment with asfotase alpha as in our case should prompt for assessment of medication compliance or treatment failure. Further assessment with detailed information about medication injections, dosage, and frequency as well as measurements of biochemical parameters, radiography, pain assessment and mobility are needed in follow up of adults with hypophosphatasia. More awareness and education on diagnosis and follow up of patients with hypophosphatasia are needed so patients can be effectively treated with available enzyme replacement therapy.

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