Case Reports

Vitamin D Dependent Rickets: Decreased Sensitivity to 1,25-Dihydroxyvitamin D


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Abstract. A patient with vitamin D dependent rickets with decreased sensitivity to 1,25-Dihydroxyvitamin D was observed. She suffered from bone pain of two years duration beginning at 12 years of age and was found to be suffering from hypocalcemia, secondary hyperparathyroidism and osteomalacia. Laboratory findings revealed normal serum 25-hydroxyvitamin D (27 ng/ml) and markedly elevated serum 1,25-dihydroxyvitamin D (131.9 pg/ml). The hypocalcemia was refractory in spite of administration of 25,000 units of vitamin D2, but therapy with high doses of oral 1α-hydroxyvitamin D3 resulted in significant elevation of the serum calcium level. The clinical findings and course of the patient’s disease were quite different from those of other patients with vitamin D dependent rickets reported by other authors.

Key words: Vitamin D dependent rickets – 1α-hydroxyvitamin D3 – Hypocalcemia – Osteomalacia

Introduction

The clinical course of vitamin D dependent rickets is similar to that of ordinary rickets due to vitamin D deficiency. However, the disease requires high doses of vitamin D throughout the patient’s lifetime. Symptoms usually begin before 2 years of age. However, there are sporadic cases in which obvious disease developed slowly and was not recognized until late in the first decade of life or even in early adulthood (Brooks et al. 1978; Harrison and Harrison 1975; Prader et al. 1961; Strewler et al. 1973). This disease may be a heterogeneous group of entities. Recent evidence suggests that the basic abnormalities is diminished renal synthesis of the active form of vitamin D-1,25-hydroxyvitamin D. Another possible mechanism that might explain the disorder is resistance of the end-organs to 1,25-hydroxyvitamin D. The patient described here had late onset osteomalacia, hypocalcemia, and secondary hyperparathyroidism in association with a normal serum concentration of 25-hydroxyvitamin D and a markedly increased serum concentration of 1,25-dihydroxyvitamin D.

Methods

The patient was evaluated as an inpatient at the Sapporo Medical College Hospital in 1977 and 1979. Twenty four-hour urine samples were collected for measurement of cyclic adenosine 3',5'-monophosphate (cAMP) and amino acids. Quantitative amino acid determination was performed by an automatic amino acid analyser (Hitachi KLA5, Tokyo, Japan). 25-hydroxyvitamin D was measured by the competitive protein binding assay method (Belsey et al. 1974). 1,25-hydroxyvitamin D was determined by radioreceptor assay method (Eisman et al. 1976). An outline of the assay method is presented in Fig. 1: assay sensitivity is 2 pg. Vitamin B12 and folic acid were determined by radioimmunoassay and competitive protein binding assay, respectively. Serum parathyroid hormone and cAMP were determined by radioimmunoassay methods.

Oral phosphorus solution was prepared and given five times daily in a total daily dose of 1.7 g (Rosen et al. 1979).

Case Report

The patient was a 14-year-old girl born after normal pregnancy: delivery and the neonatal period were uneventful. Her parents are healthy and unrelated. There was no history to suggest malabsorption, nutritional deficiency of vitamin D or steatorrhea, seizures or tetany, or of anticonvulsant drug medication. The mental state of the patient was normal.


Results

Quantitative amino acid measurement revealed generalized aminoaciduria, but serum aminocids were normal. Serum parathyroid hormone was 0.99 ng/ml (normal, under 0.50). Urinary cAMP was 28 μmol/g creatinine (normal, 2.6 to 6.5), but plasma cAMP level was normal. The plasma 25-hydroxyvitamin D was 17 ng/ml (normal, 14 to 42), and 1,25-dihydroxyvitamin D increased to 131.9 pg/ml (normal, 38.8 to 47.8). She was diagnosed as suffering from vitamin D dependent rickets. Her treatment and the clinical course of her illness are presented in Fig. 3. She was treated with daily 1α-hydroxyvitamin D₃ 1.0 μg and calcium. After 3 months of therapy the serum calcium was elevated to 8.2 and the serum phosphorus was 4.2 mg/dl. The serum alkaline phosphatase decreased to 818 mU/ml. She became free of bone pain. However, the serum calcium level decreased gradually 3 months after vitamin D₂ administration. The medication was continued for about 6 months and was stopped in order to re-evaluate the patient.

The patient was admitted to the Sapporo Medical College Hospital for the second time on March 26, 1979, 7 months after the administration of vitamin D₂ ceased. She again had a fracture of the left ulna, and a history of tetany during this period without vitamin D₂ treatment. Biochemical measurement of the serum revealed: calcium 6.6 mg/dl, phosphorus 2.3 mg/dl, magnesium 2.0 mg/dl, and alkaline phosphatase 728 μU/ml. The serum vitamin B₁₂ and folic acid were normal. Serum parathyroid hormone was 3.8 ng/ml. Urinary cAMP was

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Fig. 2. X-ray of the right knee joint. Numerous transverse lines are prominent in the terminal segments. The cortex is thin