HYPERCALCIURIC HYPOPHOSPHATEMIC RICKETS

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Abstract - A 13 year- old girl had rickets clinically evident since she was 10 years of age. She received multiple doses of vitamin D3 without improvment.

This patient manifested an unusual form of hypophosphatemic rickets with hypercalciuria. It is recommended that urinary calcium excretion be assessed in all patients with hypophosphatemic rickets before the initiation of any therapy.

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INTRODUCTION

Hypophosphatemic rickets may result from an X-linked dominant condition (also termed vitamin D resistant rickets) (1,2), renal Fanconi syndrome, renal tubular acidosis or presence of tumors that elicit a phosphaturic factor. Tieder et al, 1985 (3) and Chen et al, 1989 (4), described a hypophosphatemic bone disorder that is distinguished from other forms of hypophosphatemic bone diseases by occurrence of increased 1,25 dihydroxy vitamin D [1,25$(OH)_2$D] levels and hypercalciuria. As far as we know 33 cases have been reported in the literature. The mode of inheritance appears to be autosomal recessive and clinical manifestations range from asymptomatic hypercalciuria to severe rickets and osteomalacia (1,5). We describe a 13 year - old girl with long standing rickets and hypercalciuria. She was treated with phosphate, which resulted in clinical and radiological improvement of the rickets and marked reduction of hypercalciuria.

Case Report

A 13- year- old girl was referred for evaluation of long standing rickets. She was relatively healthy until age 10 years when fatigue, back, lower extremities, and knee pain and difficulty in walking became evident. She had bowing of both legs and epiphyseal changes of rickets were present on radiographs. Serum calcium was 10 mg/dl, serum phosphorus was 2.2 mg/dl and alkaline phosphatase 2500 IU. Vitamin D3, 600,000 unit in a single dose intramuscular per week was given for 2 weeks. Serum calcium increased to 10.7 mg/dl, serum phosphorus level became 2.3 mg/dl and no clinical or radiological improvement was noted.

A second trial of vitamin D therapy with 600,000 IU vitamin D_3/month by intramuscular injection for 3 months was given when she was 10.5 years of age. At 11.5 years of age patient received 1,25$(OH)_2$D (0.25 μg/d) plus phosphate (1.5 g/d) for one month without improvement. Patient was referred to pediatric endocrinologic clinic at the age of 13.

Both parents and her siblings were healthy. On physical examination height was 144 cm (less than the 5th percentile) and weight 40 kg (25th percentile). Bowing of both legs was evident. Breast and pubic hair development was Tanner stage 4. Laboratory data were as below.

Serum calcium 10.6 mg/dl (Nl 8.5 to 10.5 mg/dl), phosphorus 2 mg/dl (Nl 3.5-6 mg/dl). Alkaline phosphatase 2750 I.U (Nl. 200-1200) and parathyroid hormone (PTH) 7pg/ml (NL 9-55 pg/ml), 24 hour urinary calcium excretion was 6.25 mg/kg/d (NL 4 mg/kg/d). Measurment of 1-25 $(OH)_2$D was impossible in Shiraz.

Radiographically changes of rickets and osteopenia were seen. With diagnosis of hypercalciuric hypophosphatemic rickets, oral phosphate (as phosphate Sandos) therapy was begun (1.5 g/d and gradually increased to 3.5 g/d) divided into five doses. Following 4 months of treatment, the patient general health improved. Back, bone, and extremities pain and fatigue completely resolved. Laboratory data after 4 month of treatment was as below: Serum calcium 9.5 mg/dl, phosphorus 3.7 mg/dl, alkaline phosphatase decreased to 850 IU, PTH 11 pg/ml and 24 hour urinary calcium decreased to 98 mg. Radiological healing was noted.

DISCUSSION

Hypercalciuria is the hallmark of this rare form of hypophosphatemic rickets (1,3,4,6). Although this phosphate wasting disorder is clinically and radiologically similar to X-linked hypophosphatemic rickets (XLH), its distinguishing feature is the increased plasma concentration of 1,25 $(OH)_2$D which is inappropriate to hypophosphatemia (7). In classic XLH, plasma 1,25 $(OH)_2$D is low to normal (1,2). Primary renal phosphate losses incur chronic hypophosphatemia. The hypophosphatemia results in a skeletal disorder (4,7). Furthermore, phosphate depeletion increases

circulating 1,25 $(OH)_2D$, which in turn, increases the gastrointestinal absorption of both calcium and phosphorus (8).

Hypercalcemia results in hypercalciuria, nephrolithiasis and PTH suppression (8,9).

Our patient had rickets and adminstration of phosphate with no vitamin D resulted in improvement of clinical and radiological abnormalities; in addition serum phosphorus level and urinary calcium excertion returned to normal.

Urinary calcium excretion should be determined in patients with hypophosphatemic rickets, because phosphorus therapy alone appears to improve clinical, biochemical and radiographic abnormalities; in the hypercalciuric form of the disease with no risk of secondary hyperparathyroidism (10).

Vitamin D however is contraindicated because it may further increase intestinal absorption of calcium and could aggravate the patient's condition and create unnecessary complications such as kidney stones and renal damage (10). On the other hand classic XLH rickets is best managed with 1,25 $(OH)_2D$ in combination with oral phosphate (1,2).

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