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Calcium-deficiency rickets in a four-year-old boy with milk allergy

M. Davidovits, MD, Y. Levy, MD, T. Avramovitz, BSc, and B. Eisenstein, MD

From the Nephrology Unit, the Allergy/Immunology Unit, and the Department of Diet and Nutrition, Children's Medical Center of Israel, Beilinson Campus, Petah Tiqva, and the Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

A 4-year-old boy was found to have rickets associated with normal serum levels of 25-hydroxyvitamin D and high serum levels of 1,25-dihydroxyvitamin D. These findings were thought to be the result of dietary calcium deficiency caused by the prolonged elimination from his diet of cow milk and milk products because of allergy. Adequate intake of calcium resulted in rapid improvement. (J PEDIATR 1993;122:249-51)

Nutritional rickets is rare in the Western world and is mainly due to vitamin D deficiency; dietary calcium deficiency is even less common. Maltz et al.¹ and Kooh et al.² described calcium-deficiency rickets in infants receiving a prolonged special diet as therapy for chronic diarrhea. Pettifor et al.³ reported low dietary calcium levels as the cause

of rickets in rural black children in South Africa. Severe rickets was reported in three Belgian children who were fed a soy-based formula with a very low calcium content.⁴

We report a 4-year-old boy with severe rickets caused by a prolonged low calcium intake after exclusion of milk.

CASE REPORT

The patient, born in Leningrad, Russia, was the only child of healthy, nonconsanguineous Jewish parents. There was no family history of rickets. Birth weight was 3.1 kg, and the neonatal period was uneventful. Atopic dermatitis was diagnosed at the age of 2 months. The child was breast fed exclusively for 3 months. At the age of 3 months a diffuse rash developed after ingestion of a small amount of cow milk. The parents were instructed to eliminate cow milk and cow milk products from the diet and to substitute almond "milk" (mashed almonds diluted with water). The child did not re-

Submitted for publication June 3, 1992; accepted Sept. 18, 1992.

Reprint requests: M. Davidovits, MD, Nephrology Unit, Children's Medical Center of Israel, Beilinson Campus, 49 100 Petah Tiqva, Israel.

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0022-3476/93/\$1.00 + .10 9/22/42697

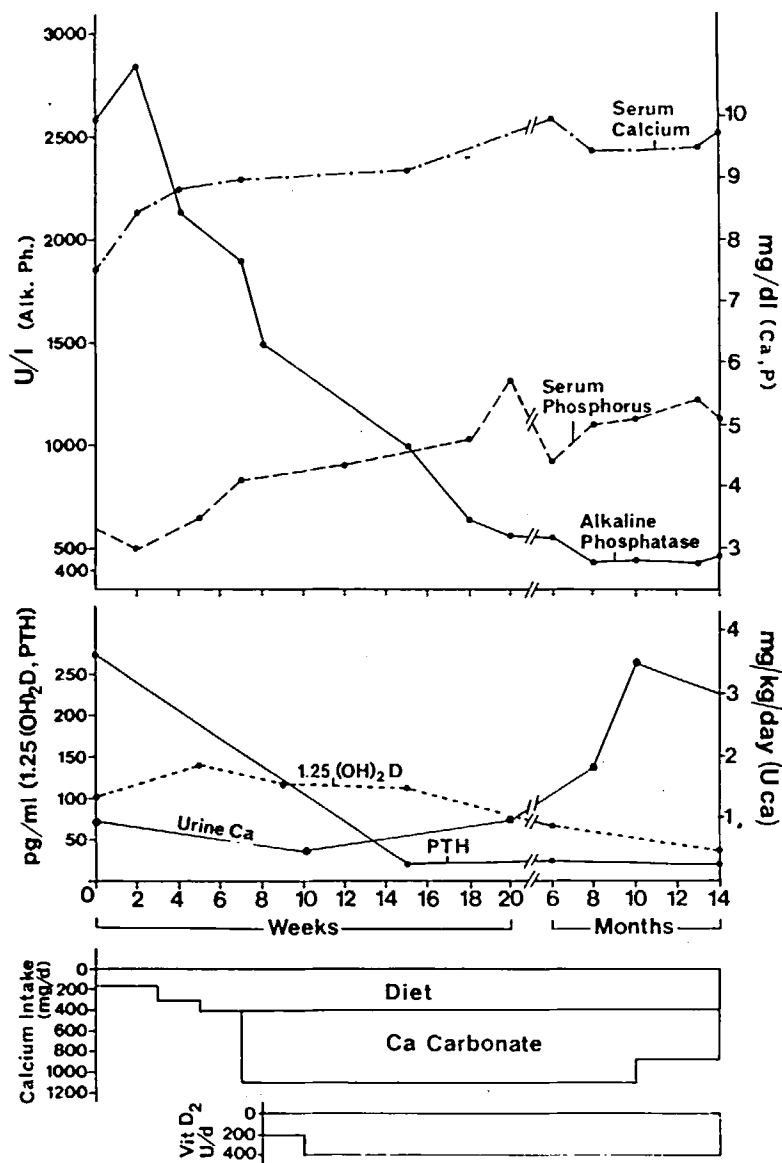


Figure. Response of biochemical and hormonal measurements to treatment. *Alk. Ph.*, Alkaline phosphatase; *1,25(OH)₂D*, 1,25-dihydroxyvitamin D; *PTH*, parathyroid hormone; *Uca*, urinary calcium.

ceive any other milk formula. Breast-feeding was stopped at the age of 1 year, and the diet included only meat, potatoes, and cabbage because of persistent eczema, presumed to result from food allergy.

When the patient was 1½ years of age, waddling gait, bowing of the legs, and enlargement of wrists and ankles were noted. Rickets was diagnosed on the basis of radiologic findings. Treatment with vitamin D was recommended but was discontinued after one dose because of the development of perioral erythema, which was interpreted as an allergic reaction. An oral cow milk challenge at the age of 2 years precipitated the immediate appearance of a diffuse rash, and continued elimination of cow milk and cow milk products from the diet was recommended. No other milk formula was given.

At the age of 4 years, the child emigrated with his parents to Israel. Physical examination revealed a small but well-nourished

child with normal mental development. Height was 4 SD below the mean and weight was at the 5th percentile for age. The head circumference was at the 5th percentile for age and appeared large in relation to height. The thoracic cage had flaring and rachitic beads. There was marked metaphyseal enlargement of the wrists, knees, and ankles, and severe genu varum. The remainder of the physical examination findings were normal.

Skeletal radiographs showed marked metaphyseal cupping and fraying at the wrists and knees, and osteopenia of the long bones. Blood chemistry tests revealed low serum calcium and phosphorus levels, 7.5 mg/dl (1.88 mmol/L) and 3.3 mg/dl (1.05 mmol/L), respectively, and high serum alkaline phosphatase activity, 2595 U/L (normal <480 U/L). The blood urea nitrogen and plasma creatinine values were normal; the plasma albumin value was 4.4 gm/dl

and magnesium 1.96 mg/dl (0.80 mmol/L). There was no metabolic acidosis. The parathyroid hormone level was 272 pg/ml (normal 10 to 55 pg/ml), with a reduced renal threshold for the maximal tubular phosphate reabsorption (normalized to glomerular filtration rate) of 2.76 mg/dl glomerular filtrate (normal 4.6 ± 0.6 mg/dl glomerular filtrate) and a reduced urinary calcium excretion of 1 mg/kg per day (normal 2 to 4 mg/kg per day). Serum vitamin D metabolite values were as follows: 25-hydroxyvitamin D, 23 ng/ml (normal 12 to 30 ng/ml), and 1,25-dihydroxyvitamin D, 103 pg/ml (normal 15 to 40 pg/ml).

Nutritional assessment revealed that the child was receiving 180 mg calcium daily. His phosphate intake was 1200 mg/day, caloric intake 80 to 90 kcal/kg per day, and protein intake 4 to 5 gm/kg per day. Prick skin tests for food allergens demonstrated strong wheal-and-erythema reactions to cow milk, egg white, soybean, peanut, and fish. After ingestion of small amounts of diluted cow milk, up to a total of 25 ml, the child had a diffuse urticarial rash, rhinitis, and conjunctival itching, all of which resolved after oral administration of corticosteroids.

The child's diet was gradually enriched with calcium of nondairy origin (dried apricots, oranges, and other fruits), up to 400 mg/day. In addition, 1800 mg of calcium carbonate was given up to a total daily elemental calcium intake of 1120 mg (Figure). Vitamin D₂ was administered first at a physiologic dosage of 200 U/day and increased to 400 U/day after 2 weeks. The phosphate intake was reduced to 800 mg/day by limiting meat in the diet.

Serum levels of calcium and phosphorus, alkaline phosphatase activity, and parathyroid hormone values were normalized 13 weeks and 8 weeks, respectively, after commencement of calcium carbonate treatment. Normalization of the level of 1,25-dihydroxyvitamin D was reached later. Urinary calcium excretion increased slowly up to 3.5 mg/kg per day, at which point the calcium carbonate dosage was reduced to 1200 mg daily (Figure). Radiographic examination of wrists and knees after 13 weeks of treatment demonstrated complete healing of rickets.

The child grew 10 cm within 12 months of treatment. The rachitic beads disappeared, wrists and ankles were no longer enlarged, and the intercondylar distance at the knees decreased from 9 to 2 cm.

DISCUSSION

The findings in this patient can be explained by prolonged dietary calcium deficiency.¹⁻⁶ The recommended daily calcium allowance at this age is 800 mg.⁷ The roughly estimated daily calcium intake in our patient was 180 mg. The main source of calcium in his diet was cabbage, which was always given together with meat. Because of the meat's high phosphate content, the absorption of this small amount of calcium was probably decreased.

The first reported cases of calcium-deficiency rickets were in two infants with protracted diarrhea who were fed a diet low in calcium but supplemented with vitamin D.^{1,2} The first infant received corn oil and meat puree, with a daily calcium intake of 36 mg. The other infant was fed a lamb-based formula with daily calcium intake of 180 mg. The South African children described by Pettifor et al.³ had

calcium-deficiency rickets because their diets contained corn with leafy vegetables, occasional eggs and meat, but no milk or milk products; the daily calcium intake was 125 mg.^{3,5,6} Three Belgian infants, because of their parents' belief that soy protein is superior to other dietary proteins, were fed a soy-based beverage marketed to treat hypercholesterolemia in adults, and calcium-deficiency rickets developed as a result.⁴

Our patient differs from the children described previously in that he had IgE-mediated cow milk allergy. Bishop et al.⁸ showed recently that cow milk allergy may not always be a transient disorder. The replacements for cow milk are usually protein-hydrolysate or soy-based formulas with adequate calcium content; alternatively, the diet is supplemented with oral calcium preparations. Our patient did not receive any infant formula or calcium substitute, probably because of the unavailability of adequate milk formulas and unawareness of the possibility of calcium-deficiency rickets.

We cannot completely exclude vitamin D deficiency in our patient, because of the low content of vitamin D in the diet and minimal exposure to sunlight in Leningrad. The normal serum level of 25-hydroxyvitamin D, observed 2 weeks after the child's arrival in Israel, could possibly be the result of the exposure to sunlight here.⁹ The rapid healing of the rachitic lesions and the rapid biochemical response to adequate intake of calcium when vitamin D was given at a maintenance dosage suggest that calcium deficiency was the main factor in the development of bone disease.

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