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Pseudo-Vitamin D Deficiency Rickets*

A Case Report

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Vitamin D resistant rickets is a well known clinical and biochemical entity, in which high doses of vitamin D is required for the treatment and the prevention of the relapse.[1] Prader et al. segregated a type of rickets under the terminology of pseudo-vitamin D deficiency rickets from vitamin D resistant rickets.[2] This entity has also been termed "deficiency type rickets due to decreased sensitivity to Vitamin D,"[3] or "vitamin D dependent rickets"[4] or "hypocalcemic vitamin-D-resistant rickets"[5].

Vitamin D-deficiency rickets is still seen in some developed countries,[6] but it is more prevalent in this part of the world.[7] [8] Therefore it is more important to differentiate pseudo-vitamin-D-deficiency rickets from simple vitamin D-deficiency cases, from the standpoint of treatment, in the countries where it is prevalent.

In this report, we present a case of pseudo-vitamin-D deficiency rickets because of the rare occurrence of this type of rickets and the age of the patient.

Case Report

A 14 year-old girl was admitted to Hacettepe Children's Hospital in January 1970 with a history of convulsions of a year's duration. She had had convulsions of 2-3 minutes duration, every 2 to 4 weeks. In spite of mysolin, diazem and epdantoine treatment her convulsions became more frequent.

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There was no history of malabsorption, but her refusal of milk and dairy products since early childhood was elucidated. The parents were first cousins and she was the fifth child of the family. An older brother had also had tetanyform convulsions and died at the age of eighteen.

Physical examination on admission revealed a pubertal, uncooperative, shy, irritable, moderately hypotonic girl in an apparently good nutritional condition. She weighed 38 kg. (3 percentile for her age) and her height was 145 cm (less than 3 percentile). With the exception of a slighly enlarged thyroid (she was from the endemic goitre area) her physical examination, including neurologic examination, was unremarkable. Trousseau's and Chvostek's signs were not elucidated. Her intelligence, as judged by the school performance was below normal range, but the I. Q. was found to be 47 (since she did not seem so dull, her impatience and shyness should be taken into consideration). There was no evidence of hypo or hyperthyroidism with the exception of dullness and irritability.

On X-ray examination, the wrist and knee revealed marked rachitic changes (Figure 1 a), chest, skull, vertebra and lamina dura of the dental alveoli appeared normal, and the bone age almost corresponded to her chronological age.

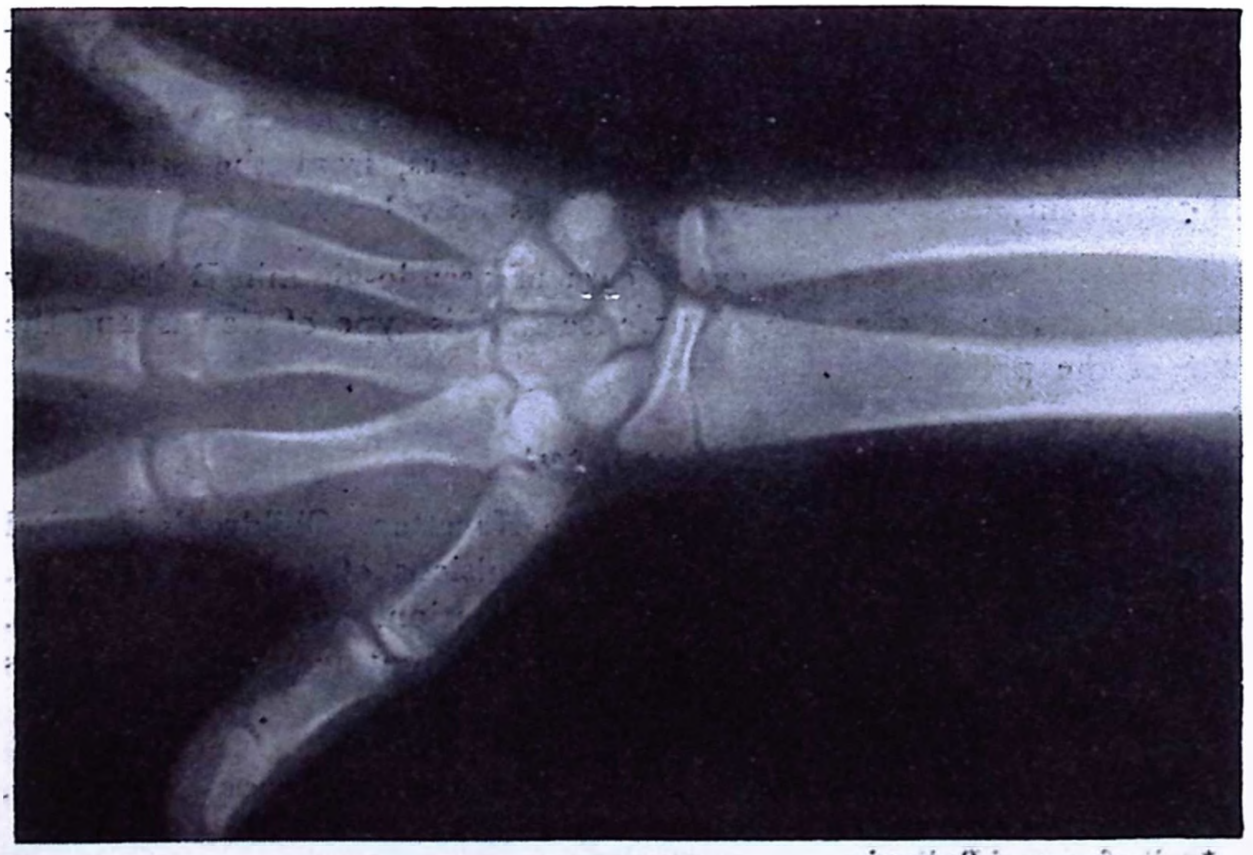

Figure 1 a
Wrist X-ray shows active rickets at the time of admission.

Laboratory examination showed Hb (14.2 gm%), hematocrit (45%), white blood cell counts (9,200/cm), serum sodium (136 mEq/L), potassium (4.2 mEq/L) chloride (95 mEq/L), carbondioxide combining power (27 mEq/L), magnesium (2 mEq/L), sugar 91% mg), NPN (32 mg%) BEI (3.1 γ/100 ml), SGOT (40 u), SGPT (14 u), CCF (+), Cholestrol (224 mg%), total lipids (810 mg%), bilirubin (0.8 mg%), thymol turbidity (1.5 u), prothrombin time (10 seconds), serum copper (74 γ/100 ml) ceruloplasmin (28 mgr/100 ml), serum proteins (Alb. 4.4 g, α_1 = 0.218 g, α_2 = 0.936 g; β = 1,7; γ = 0.863 g/100 ml); all within normal limits. Serum calcium was 6 mg %, phosphorus 4.1 mg % and alkaline phoshatase 35 B. U. An electro-encephalogram revealed centrancephalic type epileptiform activity and EKG was normal.

Microscopic examination of urine was negative and no reducing substances or protein were found. The specific gravity was 1018 and pH was 6.8. The stool did not have any abnormal appearance or frequency, the pH was 6.5 and no ova and/or parasites were seen.

Other studies: Oral, intrevaneous glucose tolerance tests, D-xylose absorption test (34.4% of D-xylose was excreted in the urine in 5 hours) and gastro-intestinal roentgenogram series were all normal. A high excretion of fat was found in the stool following daily 50 gm fat intake for three days (8.7 gm per day). Lactose loading (2 gm/kg) did not increase the blood sugar level, estimated by the Somodgji-Nelson method. However, a significant increase of blood sugar was obtained with a mixture of glucose (1 gm/kg) and galactose (1 gm/kg). (Figure 2). These results were interpreted as the indication of lactase deficiency in the intestine.

Urinary dilution, concentration and creatinine clearance tests were normal, so was the urinary acidification by loading with 0.1 gm/kg ammonium chloride (pH went down from 6.8 to 4.5) and amino aciduria determined as an alpha amino nitrogen (7.2 mg/24 hours). An IVP, besides the double collecting system on the right kidney, was interpreted as within normal limits.

Calcium infusion (test 20 mg/kg calcium gluconate for a period of 4 hours) resulted in an early increase of serum calcium, but daily excretion of calcium and phosphorus was not markedly changed (22 mg calcium and 193 mg of phosphorus were found in her 24 hours urine during calcium infusion).

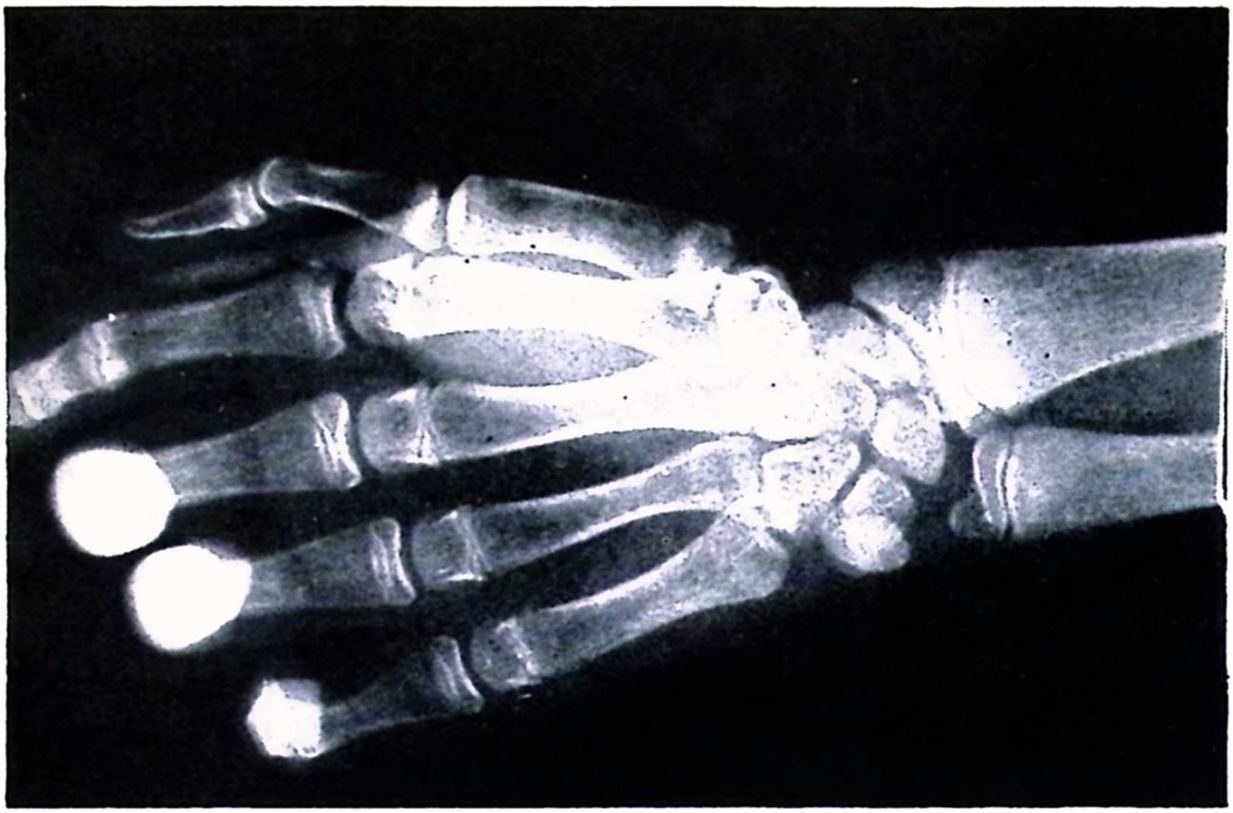

Figure 1 b

X-ray of the wrist, on the 65th day of treatment, shows complete disappearance of rachitic changes.

Course :

In view of these laboratory facts we believed that this was a case of pseudo-vitamin-D-deficiency rickets and high doses of vitamin D was started (50,000 units) with 8 gm calcium lactate daily. Phenobarbital (5 mg/kg) was added as an anticonvulsive medication. Because her serum calcium level increased to low normal level by the 34th day of treatment, calcium lactate was discontinued. On the 65th day of treatment vitamin D was decreased to 40,000 u per day and to 20,000 u per day on the 95th day of treatment. On the 65th day of treatment the X-rays of the wrist and knee showed complete disappearance of rachitic changes (Figure 1b). On the 125th day of treatment when she was on vitamin D 20,000 u/daily, her serum alkaline phosphatase was found slightly raised and vitamin D was increased to 40,000 u. The chemical findings of rickets were reversed on her last visits. (Table 1) She has had two fractures with minor traumas since her first admission to this hospital. In the interim, although her convulsions became less frequent and shorter, her EEG findings were not changed and she was given epdantoine.

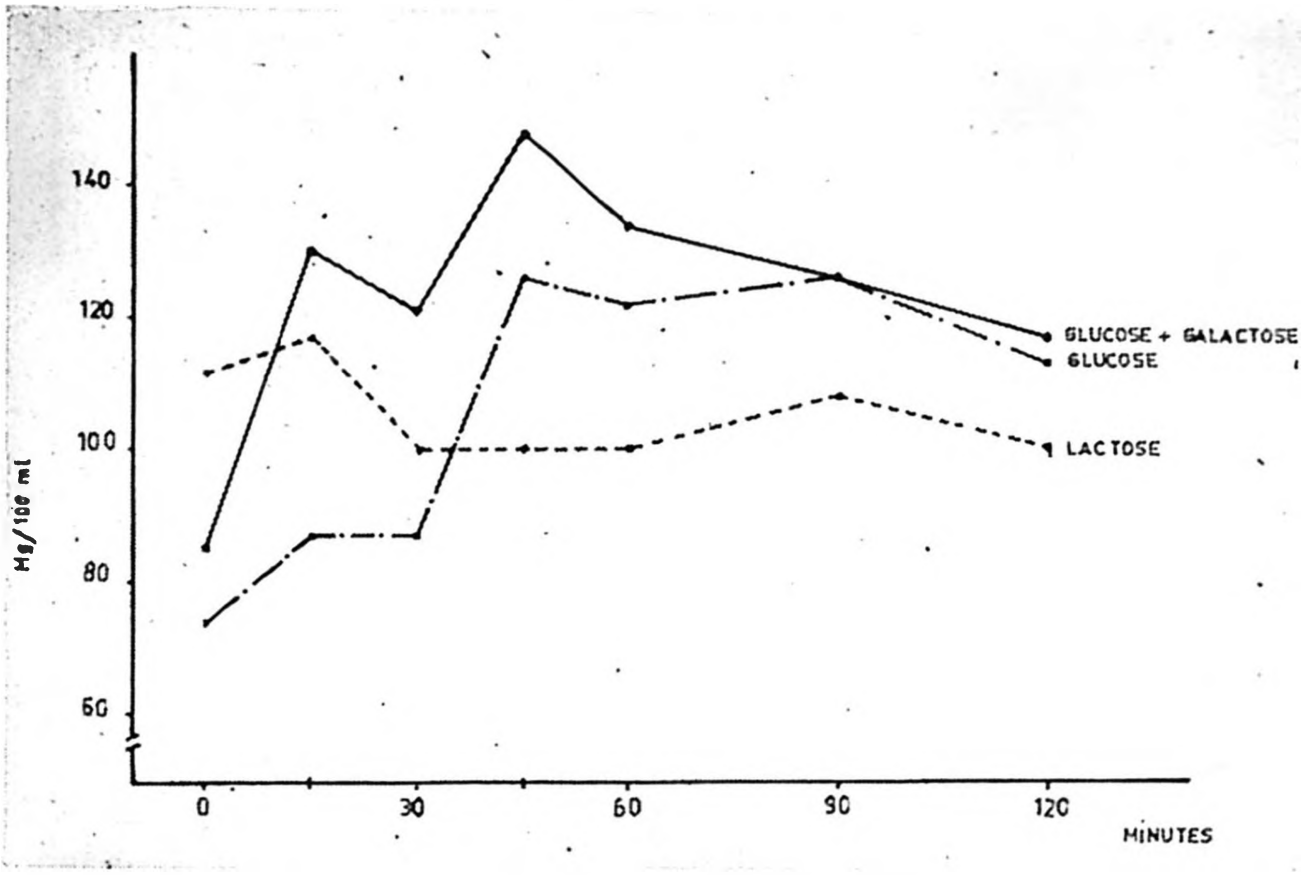

Figure 2
Glucose, lactose (2 gm/kg) and glucose (1 gm/kg) + galactose (1 gm/kg) absorption studies are indicated.

TABLE I

CALCIUM, PHOSPHORUS AND ALKALINE PHOSPHATASE CHANGES DURING VITAMIN D TREATMENT

The day of treatment	Ca+ (mg %)	P (mg %)	Alkaline phosphatase (B. U.)
On admission	6	4.1	35
34th day	8.1	4.4	31.8
65th day	10.8	5.6	18.6
95th day	10.8	5.4	14.6
125th day	10	5	21
168th day	10.2	7	11.2
199th day	10	4.6	10.8

Most of the studies were repeated on her last admission (125th day of treatment) which revealed normal kidney functions (dilution concentration; acidification of urine by ammonium chloride, creatine clearance). The calcium infusion on this occasion showed marked calciuria (7 mg/day prior to and 222 mg/day during), but no changes in phosphate excretion (prior to 325 mg and during 338 mg). Blood sugar was not changed at all during lactose tolerance test.

Discussion

This patient had all the chemical and x-ray evidences of rickets. The calcium infusion test[9] showed 97 per cent retention at the time of admission when her rachitis was active, and 71 percent retention when her disease improved radiologically and chemically. This was further evidence of her active rickets, as she did not have osteomalacia.

The classical form of vitamin-D resistant rickets is a hereditary disease and usually becomes symptomatic in the first two years of life. It is always normocalcemic and hypophosphatemic and requires much larger doses of vitamin D than this patient had received for the treatment. Other causes of rachitis, such as liver and kidney diseases, were ruled out with the appropriate tests. At this age it is unlikely that rickets would be due to vitamin-D-deficiency, even if malabsorption is present. Normal response to ingested glucose, galactose and D-xylose demonstrates that at least three absorptive pathways involving the proximal small intestine were intact where calcium absorption occurs mostly. The roentgenologic findings and increased alkaline phosphatase level might be explained by hyperparathyroidism, but low serum calcium, lack of hyperphosphaturia, normal serum phosphorus and the normal dental alveolar appearance on x-ray were against this diagnosis. In spite of hypocalcemia, hypoparathyroidism was not taken into consideration because of rachitic changes and normal serum phosphate. Since her electrolytes were normal Albright syndrome was not considered.

Clinical and metabolic features common to pseudo-vitamin-D deficiency rickets which are hypocalcemic tetany, normal or slightly diminished serum inorganic phosphate, absence of hyperphosphaturia, increased activity of alkaline phosphatase, growth retardation, aminoaciduria, hypotonicity, irritability, convulsive seizure suggesting hypocalcemic tetany, dull mentality and early onset of rickets,[2 10 11 12] are consistent with those of our patient. The oldest patient previously diagnosed as having pseudo-vitamin-D-deficiency rickets was an 11 year old Japanese boy.[10] Although this patient is much older for this kind of rickets her marked growth retardation might suggest that her disorder started much earlier than learned from her history.

The large variability of vitamin D requirement and the age of the patients with this disorder,[3 4 12] may indicate that the severity of pseudo-vitamin D deficiency rickets, changes from patient to patient. The mild low intelligence of our patient, as judged by her performance in school, I. Q. level and convulsions are compatible with the diagnosis. It is

possible, of course, that convulsions were due to other causes. If her older brother had the same kind of tetanyform convulsions, we might suppose he also had had pseudo-vitamin D deficiency rickets which fits the heredity of this disorder.

Despite the normal vitamin D activity in the serum of these patients,[3 4] specific calcium malabsorption has been shown.[4 10] Vitamin D absorption is probably normal since serum antirachitic activity increases with the increasing oral doses of vitamins.[4] Although magnesium and calcium absorptions are related,[14] the former's absorption is not changed markedly in this condition.[4] The serum magnesium level of our patient was also found normal in spite of marked hypocalcemia. Although some evidence of fat malabsorption was found, she did not have clinical or laboratory findings of deficiency of other vitamins emulsified in the fat. Fat malabsorption was also documented in Soriano et al's case whose absorption defect was partially corrected following vitamin D treatment.[3]

Intestinal lactose deficiency demonstrated by defective lactase absorption was also shown in Matsuda et al's[10] patient as it was in this case. In the light of recent studies of Condon et al[13] one might relate hypocalcemia to lactose deficiency. The correction of hypocalcemia and rickets in this patient in a relatively short period of time by oral administration of vitamin D, without any changes in lactose absorption (as it was shown in Matsuda et al's case,[10] indicates that lactase deficiency is not related to the pathogenesis of this disorder.

In spite of marked rickets, hyperphosphaturia was not found in this girl as recorded in this disease by others,[4 10 11] and hyperaminoaciduria was not present as in Soriano et al's patient.[3]

Summary

A 14 year old girl with rickets, hypocalcemia, hypotonia, irritability, absence of hyperphosphaturia, seizure, growth retardation was presented as another case of pseudo-vitamin D deficiency rickets. She also had lactose intolerance. Her hypocalcemic rickets was treated in a relatively short period of time with high doses of vitamin D on which she was found dependent.

Acknowledgements

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