Discussion

In adults prostatic calcification is often found in association with prostatic hypertrophy. Fox¹ reviewed 3510 patients who had been examined radiologically and found that 484 (13.8%) had prostatic calculi, the youngest patient being 16 years.

The history of rickets in this patient for which unknown amounts of vitamin D and calcium had been given might explain the prostatic calcification, as this is most unusual in so young a patient. The child was symptom-free when he came to our surgical unit and there was no sign of back pressure from either the prostatic calcification or the ureteric

stone. Whether this boy will have any future complications from his prostatic calcification remains to be seen.

I thank Dr Modhafer Saeed for referring the patient, and Dr Issam Al-Hatem for performing the radiology.

Reference

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Correspondence to A Y Izzidien FRCS, Department of Surgery, Medical College, Ninevah, Iraq.

Late presentation of vitamin D-dependent rickets

JENNIFER COWEN AND F HARRIS

Department of Child Health, Alder Hey Children's Hospital, Liverpool

SUMMARY An 8½-year-old girl presented with rickets. This had developed despite a normal diet and in the absence of symptoms, signs, or laboratory evidence of malabsorption, hepatic or renal disease. The rickets healed with physiological doses of 1- α -hydroxy-cholecalciferol. It is suggested that this case provides evidence for genetic and metabolic heterogeneity in vitamin D-dependent rickets.

Vitamin D-dependent rickets (pseudo deficiency rickets) is a rare but well recognised inborn error of cholecalciferol (D_3) metabolism, which presents classically in the first year of life. Prader *et al.*¹ were the first to describe infants with muscular hypotonia, retarded growth and development, hypocalcaemic tetany, and severe rickets. Such patients have low concentrations of serum calcium, low or normal serum inorganic phosphate, raised serum alkaline phosphatase, high serum parathormone, and a generalised aminoaciduria. The underlying defect is thought to be an inability in the kidney to achieve hydroxylation of 25 (OH) cholecalciferol to 1,25 (OH)₂ cholecalciferol. This is inherited as an autosomal recessive. Recently it has been suggested that the condition is heterogeneous and that there may be more than one defect in the metabolism of 25 (OH) D_3 to 1,25 (OH)₂ D_3 and its subsequent action on the gut. The patient reported here presented relatively late and lends some support to the latter hypothesis.

Case report

This 8½-year-old white girl presented with a short

history of fever, paraesthesia in her fingers, and tetany. No other symptoms were elicited. Her diet was normal. Her past medical history was normal, except for gross obesity in infancy. Weights recorded at the local welfare clinic include 10.5 kg at 4½ months, 14 kg at 10 months, and 16.4 kg at 16 months. The diet consisted of full cream Cow and Gate milk at 5 months and a good mixed diet thereafter. On examination she was febrile, with a red throat, and cervical lymphadenopathy. She exhibited carpopedal spasm but Chvostek's sign was negative. There was no clinical evidence of rickets, enamel hypoplasia, or muscle hypotonia. She was above the 50th centile for height and the 90th centile for weight. Her father is 188 and her mother 156.7 cm tall. No other abnormality could be detected.

Her tetany responded rapidly to 20 ml of 10% calcium gluconate given intravenously. Blood was then taken for analysis (Table). Her urine chromatogram showed gross generalised aminoaciduria. She showed no proteinuria or glycosuria. X-ray films of the left wrist and hand showed active rickets, with no evidence of hyperparathyroidism.

Further investigation did not show any biochemical evidence of malabsorption, nor any sign of renal or hepatic disease (Table). The patient was started on 10 000 units of calciferol BP and 8 g calcium gluconate daily (Figure). She remained asymptomatic.

After 3 weeks of treatment her serum calcium was 2.09 mmol/l (8.4 mg/100 ml) and her serum inorganic phosphate 2.02 mmol/l (6.1 mg/100 ml). The aminoaciduria had resolved and x-ray films showed some bone healing. The calciferol was stopped and her biochemistry promptly deteriorated.

Figure Variation of calcium and alkaline phosphatase with treatment.

Table Results of some investigations

	Patient	Normal
Serum		
Calcium	1.6 mmol/l	
Phosphate	1.7 mmol/l	1.1–1.9 mmol/l
Alkaline phosphatase	28 KA units	
Magnesium	0.80 mmol/l	
Serum parathormone	5 ng/cm ³	Less than 1.0 ng/cm ³
25-Hydroxy-vitamin D3	14.1 ng/ml	4–20 ng/ml
Haemoglobin	12.9 g/dl	
Urea and electrolytes	Normal	
Plasma bicarbonate	24 mmol/l	
Serum creatinine	70 µmol/l	
Total serum protein	68 g/l	
Albumin	43 g/l	
Serum aspartate transaminase	Less than 10 IU/l	
Xylose and glucose tolerance tests	Normal response	
Blood gases (finger prick)		
pH	7.37	
PCO ₂	41 mmHg	
Base excess	–1 mmol/l	
Standard bicarbonate	23 mmol/l	
Urine osmolality	409 mmol/kg	
Midstream urine	No growth	

Conversion: SI to traditional units—calcium 1 mmol/l ≈ 4 mg/100 ml, phosphate 1 mmol/l ≈ 3.09 mg/100 ml, magnesium 1 mmol/l ≈ 2.4 mg/100 ml, creatinine 1 µmol/l ≈ 0.0113 mg/100 ml.

Within a month her calcium had fallen to 1.89 mmol/l (7.5 mg/100 ml) with a corresponding rise of her alkaline phosphatase to 43 KA units. Four days after restarting calciferol 10 000 units a day, after a 3-month period without any treatment, her 25 (OH) D₃ was 163 ng/ml and her parathormone 10 ng/cm³. Calciferol 10 000 units per day was continued. After one month of treatment there was again an improvement in her serum calcium to 2.3 mmol/l (9.2 mg/100 ml). The calciferol was withdrawn once more and during the next 2 months the child's calcium fell to 1.79 mmol/l (7.2 mg/100 ml). At this time her plasma parathormone was 10 ng/cm³, and her plasma 25 (OH) cholecalciferol was 51.0 ng/ml, both above the upper limit of the normal range. The patient was started on 0.5 µg

1-α-hydroxy-cholecalciferol (one-alpha, Leo) daily. This dose was subsequently increased to 1 µg daily. She has been on this treatment for 11 months and has remained well with normal biochemistry. There is no radiological evidence of rickets. Recent investigations show serum calcium 2.38 mmol/l (9.5 mg/100 ml), phosphate 1.96 mmol/l (6.0 mg/100 ml), and alkaline phosphatase 26 KA units. Her urinary amino-acid pattern is normal. Serum parathormone was 1.7 ng/ml, measured after 5 months' treatment with 1 µg 1-α-hydroxy-cholecalciferol.

Discussion

The history, biochemistry, and clinical course of this child show that her rickets was not due to nutritional deficiency of vitamin D, malabsorption, or to chronic renal or hepatic disease. Although coeliac disease and other malabsorption states cannot be ruled out without further investigation, it is felt that these tests were not indicated in the face of such evident wellbeing, growth, and development. Furthermore, the child's response to an oral physiological dose of 1-α-hydroxy-cholecalciferol provides good evidence against these conditions. She lacks the features essential for familial hypophosphataemic rickets. Thus the most likely diagnosis is a mild variant of vitamin D-dependent rickets. It has been suggested that the primary defect is a failure of 1α hydroxylation of 25 OH D₃ in the kidneys, so such patients should respond to large doses of calciferol or to physiological doses of 1,25 (OH)₂ D₃. However, heterogeneity of the condition has been suggested by the variable response of 3 patients to dihydro-tachysterol.² One child responded well to dihydro-tachysterol but 2 others, who were brothers, did not respond at all. Consequently it was concluded that all patients with this syndrome did not necessarily have the same autosomal recessive trait and 'that the

metabolic block is differential and variable'. Balsan *et al.*³ thought that the slightly greater requirement of patients with vitamin D-dependent rickets for 1 α -hydroxy D₃ compared with vitamin D-deficient patients threw some doubt on the site and type of the metabolic block in the former condition. They suggested that this might be due to factors related to the severity of 25 hydroxy D₃ 1- α -hydroxylase deficiency.

In infants of similar age and size Balsan *et al.*⁴ reported a range of dosage requirements of cholecalciferol (D₃) from 600 to 7660 μ g daily. Although most patients with vitamin D-dependent rickets who have been described so far have required large doses of cholecalciferol, Rosen and Finberg² mentioned one child who was maintained on 1000 IU/24hours (20 μ g) 25-OH D₃.

It might be expected that if the defect were less severe the presentation of affected patients would be later, and this is borne out to some extent in the reports. The majority of patients who have been reported were between 1 month and 2 years when they first came to medical attention and they have required up to 100 000 IU (2.5 mg) D₃ daily. The patient of Rosen and Finberg,² who required 3500 IU (87.5 μ g) D₃ daily, did not present until he was aged 4½ years when his main symptom was clumsiness. An even older patient (14 years) in that series was

investigated because he was the sibling of an affected infant. He was maintained on a relatively small dose of 5000 IU (100 μ g) 25-OH D₃ daily.

It would seem that our patient has relatively mild disease and therefore presented late. Nevertheless, in common with more severely affected individuals she requires the physiological dose of 1 μ g 1- α -hydroxy-cholecalciferol daily.

References

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Correspondence to Dr Jennifer Cowen, Department of Child Health, Alder Hey Children's Hospital, Eaton Road, Liverpool L12 2AP.

Zinc-dependent chemotactic defect in an infant with acrodermatitis

L BUSINCO, A M MENGHI, P ROSSI, R D'AMELIO, AND E GALLI

First Department of Paediatrics and Second Department of Infectious Diseases, University of Rome

SUMMARY A 5-month-old infant developed acrodermatitis enteropathica when weaned from breast milk to cows' milk. Plasma zinc concentration was low. T- and B-lymphocyte functions were normal, but there was a severe defect of neutrophil chemotaxis. Oral treatment with zinc sulphate (40 mg daily) induced an immediate clinical improvement, with restoration of normal plasma zinc level and complete correction of neutrophil chemotaxis.

Acrodermatitis enteropathica (AE) is an autosomal recessive inherited disorder characterised by diarrhoea, failure to thrive, anorexia, a vesiculobullous eruption around the mouth, anus, hands, and feet, alopecia, photophobia, paronychia, and high susceptibility to *Candida albicans* and *Pseudomonas aeruginosa* infections. The disease can appear when the infant is weaned from breast milk to cows' milk. In the untreated child death results from overwhelming infections, superimposed on a chronic

marasmic state. Until a few years ago treatment was empirical, and consisted of breast-milk feeds and the oral administration of halogen-substituted 8-hydroxy-quinolines.¹ In 1975 Moynahan² reported low levels of zinc in the plasma of AE patients and the successful treatment of the disorder with oral zinc salts, which brought about both an increase in the plasma zinc and clearance of symptoms. Eckhart *et al.*³ suggested that the disorder might be related to zinc metabolism, with low quantities of certain zinc-binding ligands of low molecular weight, which are essential for the absorption of the metal, and protect it from chelation by other dietary components. The immune system of affected children has shown various anomalies: delayed-hypersensitivity skin reactions negativity, lack of serum IgA and IgM and, more recently, neutrophil and monocyte chemotaxis defect.⁴⁻⁶

We report an infant with AE who also had a severe neutrophil chemotaxis defect in the presence of normal intrinsic motile capacity. A striking