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Osteomalacia associated with increased renal tubular resorption of phosphate (hypohyperparathyroidism)

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Summary

A 12-year-old girl, who presented with joint pains, was found to have hypocalcaemia, hyperphosphataemia due to increased renal tubular reabsorption, increased serum alkaline phosphatase activity, and osteomalacia. These features, which resemble those found in so-called hypohyperparathyroidism, were all rapidly reversed by small doses of cholecalciferol.

Introduction

Costello and Dent (1963) suggested the term hypohyperparathyroidism to describe the apparent co-existence of parathyroid overactivity and diminished renal responsiveness to parathyroid hormone (PTH) in a seven-year-old girl with normal glomerular function and with no stigmata of pseudohypoparathyroidism. Biochemical hypoparathyroidism was inferred from the low serum calcium (Ca) and high serum inorganic phosphate (Pi), whilst typical X-ray changes and increased activity of serum alkaline phosphatase (SAP) suggested parathyroid overactivity. Allen, Millard and Nassim (1968) reported increased osteoid in a bone biopsy specimen from a similar patient. Recently, a twelve-year-old girl with similar features has been studied, and her response to cholecalciferol is reported.

Case report

A 12-year-old female Indian immigrant, who had lived in Scotland for the previous 4 years, presented in April 1973 with a 4-week history of pain

in the knees. She had previously been in good health and her menstrual periods had just begun. She was of normal height (150 cm) and weight (40 kg), and secondary sex characteristics were present. Chvostek's sign was present but there were no other abnormal features on examination.

Results of investigations were as follows: chromosomal karyotype was that of a normal female; serum Ca was low and plasma Pi was increased (Table 1); SAP activity was 427 iu/l, which is markedly elevated for a girl of this age (Clark and Beck, 1950; Round, 1973), and qualitative electrophoresis showed that this increased activity was of bony origin; plasma urea, creatinine, magnesium and other electrolytes were normal; there was no amino-aciduria, glycosuria or proteinuria; the urinary excretion rate of calcium was very low, 0.7 mEq/24 hr; the estimated maximum renal tubular resorption of phosphate per unit of glomerular filtration rate (T_{mp}/GFR) (Bijvoet and Morgan, 1971) was markedly elevated (Table 1); urine acidity after oral ammonium

TABLE 1. Investigations before and during treatment with cholecalciferol

	Before treatment	After 6 weeks of treatment	Normal adult range
Serum Ca (mEq/l)	3.4	4.5	4.5-5.0
Plasma Pi (mg/100 ml)	6.0	4.9	2.7-4.5
SAP (iu/l)	355	210	25-85
Serum 25-OHD (ng/ml)	<0.8	25	4-23
Serum PTH (ng/ml)	2.0	<0.9	<0.9
T _{mp} /GFR (mg/100 ml)	7.4	4.2	2.5-4.2

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FIG. 1. Serial determinations of serum Ca, plasma Pi and SAP before and during treatment with cholecalciferol.

chloride (Wrong and Davies, 1959) and urine osmolarity after overnight fluid deprivation were normal.

X-rays of the hands and wrists showed normal bone age but widening of the radial and ulnar epiphyses and sub-periosteal erosions of the phalanges; examination of a bone biopsy specimen from the iliac crest revealed abnormally wide osteoid seams on trabecular surfaces, characteristic of osteomalacia; there was evidence of active bone formation and resorption but not of osteitis fibrosa.

Serum 25-hydroxy vitamin D (25-OH D) (Preece *et al.*, 1974) was undetectable when serum immunoreactive PTH (Addison *et al.*, 1971) was elevated and serum calcium was low (Table 1); there was no evidence of generalized intestinal malabsorption; daily dietary intake was estimated to be 1.7 g of Ca, 1.9 g of P and 5 µg of vitamin D.

Treatment with cholecalciferol, 50–75 µg daily, led to a rise in serum Ca and a fall in plasma Pi and SAP (Fig. 1). Six weeks after beginning treatment, she was symptom-free, and Tmp/GFR, serum PTH and serum 25-OHD were all normal (Table 1). Following an injection of PTH, urinary cyclic-AMP excretion increased from 2.0 to 22.7 nmol/min, suggesting that the renal response to PTH was normal at this stage (Chase and Aurbach, 1967). Eight months after starting treatment, hand and wrist X-rays were normal.

Discussion

The main clinical features of this patient were very similar to those of two previously reported cases of hypohyperparathyroidism (Costello and Dent, 1963; Allen *et al.*, 1968). Development was normal, there

was hypocalcaemia, hyperphosphataemia and increased SAP activity, X-rays showed rachitic changes and cortical erosions, and there was histological evidence of osteomalacia in the two patients on whom bone biopsies were performed. Such changes are found in chronic renal failure and pseudohypoparathyroidism, but there was no evidence of either condition in these patients.

Since the assay for vitamin D measures the 25-hydroxy derivatives of both D₂ and D₃, the low serum level, in the absence of intestinal malabsorption syndrome, suggests that this patient had a dietary deficiency of vitamin D, and that the dietitian's assessment was in error.

The pre-treatment plasma Pi (mean 5.6 mg/100 ml) is probably within the normal range for a girl of this age (Greenberg, Winters and Graham, 1960; Round, 1973) but is unexpectedly high in a patient with vitamin D deficiency and secondary hyperparathyroidism. This high plasma Pi was due to a high setting of renal tubular resorption, suggesting unresponsiveness of the renal tubule to PTH, such as occurs in the inherited condition of pseudohypoparathyroidism. The fall in plasma Pi when the patient was given cholecalciferol, suggests that in her case such end organ resistance was acquired and secondary to vitamin D deficiency.

Decreased renal sensitivity to PTH could be due to altered metabolism of vitamin D, the hydroxylated derivatives of which may have a permissive role in the renal tubular action of PTH (Holick and DeLuca, 1974). Hypocalcaemia itself may increase renal tubular resorption of Pi, as suggested by the observation that the renal tubular response to PTH may be restored by Ca infusion in some patients

with pseudohypoparathyroidism (Rodriguez *et al.*, 1974).

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Diffuse vasculitis, eosinophilia, and elevated antibody titre to measles virus

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Summary

In the original description of serum sickness by Von Pirquet and Schick (1905) vasculitis was described as a feature. This was subsequently shown to be due to circulating immune complexes, which are known to be eosinotactic. The following report describes a case of serum sickness, occurring in a 14-year-old boy, characterized by diffuse vasculitis with communicating hydrocephalus and accompanied by a pronounced eosinophilia. A significantly raised antibody (IgG) titre to measles virus was demonstrated in his serum and

indicated that this agent probably provided the initial antigenic stimulus.

Case report

A 14-year-old white boy of English parentage was admitted as an emergency to the Royal United Hospital, Bath, with a 24-hr history of abdominal pain. This was originally central in position but subsequently radiated to the right iliac fossa. He had also had pain in both sides of the neck. One month before the onset of these symptoms he had had a sore throat and non-productive cough, but no rash. From that time he had remained anorexic and lethargic. There was no previous history of illness except for mild eczema at the age of 2.5 years; this did not persist and there were no other atopic features. He had had a dry scaly skin since birth and one of his four sisters was similarly affected. He had neither had

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