MEDICAL MEMORANDA

Alkali Treatment of Renal Osteodystrophy

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Although chronic renal failure is frequently complicated by metabolic acidosis and bone disease, the relation between them is controversial (Kyle, 1969; Stanbury, 1970). We report a case in which renal osteodystrophy was reversed by alkali treatment alone.

Case Report

In 1960 a 5-year-old girl was found to have developed accelerated hypertension (B.P. 190/150) with blood urea 119 mg/100 ml. An intravenous pyelogram showed a small scarred left kidney (5.3 by 3.2 cm). There was also upper pole scarring with clubbed calyces on the right side. Left nephrectomy was performed and histological examination of the kidney confirmed pyelonephritic changes, and showed infiltration of the submucosa of the renal pelvis and ureter with inflammatory cells. Blood pressure fell for six months. It subsequently became raised, and was controlled by guanethidine 10-25 mg/day. Urine cultures were occasionally positive but long-term sulphadimidine controlled these episodes. From 1961 until 1970 the blood urea varied between 45 and 60 mg/100 ml.

In July 1969 she developed pain in the shins on walking, and was found to have a plasma alkaline phosphatase of 39 K.A. units with calcium 9.2 and phosphate 3.3 mg/100 ml. X-ray pictures of both tibiae showed no evidence of bone disease. Her symptoms continued to trouble her, and she was admitted to hospital in April 1970 for further investigation.

On examination she appeared fit with well-developed secondary sexual characteristics. Her height was 161 cm (50th percentile; unchanged for nine months before admission). Measurements of her segments were crown to pubis 76 cm, pubis to heel 85 cm, span 168 cm. There was no proximal muscle weakness, but her bones were tender, and both tibiae slightly bowed.

Investigations were: plasma urea 55 mg/100 ml, sodium 135 mEq/l., potassium 3.2 mEq/l., chloride 110 mEq/l., CO₂ 18 mEq/l., calcium 9.0 mg/100 ml, phosphorus 2.7 mg/100 ml, alkaline phosphatase 52 K.A. units/100 ml, non-protein-bound hydroxyproline 3.7 mg/l. (normal < 2.9); creatinine clearance 41 ml/min (corrected for body surface area 1.73 m²); midstream specimen of urine was sterile; trace protein, glucose, amino-acids; 24-hour urine calcium 32 mg, phosphorus 720 mg. Urine acidification test showed minimum urine pH 6.5, maximum total acidity 38.0 μEq/min (normal > 60), titrable acidity 6.1 μEq/min (normal > 25), ammonium 31.9 μEq/min (normal > 35). Arterial blood pH (before acid load) 7.24, base deficit 10 mEq/l. A bone x-ray film showed a typical "rugger-jersey" spine but no other abnormalities. The appearances of cancellous bone from the iliac crest biopsy specimen were typical of osteomalacia (maximum number osteoid lamellae 7, surface coverage 75%) and osteitis fibrosa (increase in number of resorptive areas, excess surface fibrosis, irregular cement lines).

She was discharged without specific treatment. On her re-admission three months later she had more bone pain, and the creatinine clearance had fallen slightly to 29 ml/min. The defect in urinary acidification was still present and plasma alkaline phosphatase

was raised. Plasma hydroxyproline had risen to 9.2 mg/l., suggesting further increase in bone resorption (Bishop and Smith, 1971). There was a positive calcium balance of 150 mg/day and zero phosphorus balance. Treatment was begun with sodium bicarbonate (6 g/day).

After seven months on this regimen she no longer had bone pain. The creatinine clearance was unchanged. Plasma, calcium, phosphorus, hydroxyproline, and bicarbonate were within normal limits. Plasma alkaline phosphatase had fallen to just above normal (14.0 K.A. units/100 ml). Bone biopsy showed only a few small foci of osteoclastic resorption, with no osteomalacia or surface fibrosis. Further metabolic balance studies showed slight negative calcium and zero phosphorus balance.

Nine months later iliac crest bone biopsy showed normal cancellous bone. Plasma biochemistry and x-ray appearances were unchanged.

Comment

Although this patient had functional renal tubular disease evidence suggests that the osteodystrophy was more typical of renal *glomerular* failure. X-ray pictures showed osteoclerosis, and the bone biopsy showed osteitis fibrosa besides osteomalacia. Furthermore, resorptive bone disease was suggested by the raised plasma non-protein-bound hydroxyproline. On alkali therapy acidosis was corrected, symptoms were relieved, plasma alkaline phosphatase and hydroxyproline fell, and follow-up bone biopsies showed healing of osteomalacia and osteitis fibrosa, despite paradoxical changes in calcium balance.

Alkali therapy alone may cure osteomalacia or rickets as associated with the acidosis of primary renal tubular disease (Foss *et al.*, 1956) or uretero-colic anastomosis (Green and Boyd, 1959), but its efficacy in azotaemic osteodystrophy has been doubted. Although a cumulative depletion of calcium from bone may arise through the additional requirement for bone mineral buffer in acidotic renal failure (Lennon, 1969) there is no evidence that such losses cause bone disease.

Plasma alkaline phosphatase (Sereny and McLaughlin, 1970) and bone histological appearances can both vary with skeletal growth rather than bone disease. Although this patient was adolescent she had stopped growing, and her epiphyses were fused before the period of study. It is possible that renal osteodystrophy can improve spontaneously but we cannot make this assumption in the absence of serial data on untreated renal osteodystrophy.

The evidence suggests that acidosis was a notable cause of osteodystrophy in this patient, and alkali therapy rather than cessation of skeletal growth or spontaneous remission led to its cure.

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