Severe hypophosphataemic osteomalacia with primary hyperparathyroidism

Osteomalacia is rare in primary hyperparathyroidism. Characteristically, the serum calcium concentration is normal in primary hyperparathyroidism complicated by vitamin-D-deficient osteomalacia but hypercalcaemia develops quickly after administration of vitamin D.1

We have studied a patient with hypercalcaemic primary hyperparathyroidism who presented with hypophosphataemic osteomalacia. Vitamin D treatment produced a rise in serum inorganic phosphate concentration associated with bone healing but no consistent change in serum calcium concentration.

Case report

The patient, a 48-year-old married woman with no previous illness, presented in 1973 with an eight-month history of diffuse and severe bone pains, weakness and muscle wasting, and difficulty in walking. She was unable to stand erect from the sitting position. Pressure applied to her ribcage produced spontaneous severe pain. Skeletal x-ray films showed multiple rib fractures but no obvious subperiosteal erosion. Bone histology showed severe osteomalacia with osteoid 29%, total trabecular bone volume (equivalent to 85%), bone matrix. Plasma concentrations were: calcium 3.2 mmol/l (12.8 mg/100 ml), inorganic phosphate 0.5 mmol/l (1.5 mg/100 ml), creatinine 60 µmol/l (0.7 mg/100 ml), magnesium 0.76 mmol/l (1.8 mg/100 µl), alkaline phosphatase 20 KA units, parathyroid hormone 19 ng/ml (normal up to 1.0 ng/ml), and 25-hydroxy vitamin D 33 nmol/l (11 ng/ml) (normal 13-88 nmol/l; 5-35 ng/ml). A 24-hour collection of urine contained hydroxyproline 560 µmol/l (7.8 mg/100 ml), calcium 3.02 mmol/l (12 mg/100 ml), and inorganic phosphate 10% mmol/l (36 mg/100 ml). Dietary vitamin D intake was normal. A jejunal biopsy specimen and barium studies of the small bowel were normal. Hyperparathyroidism with osteomalacia was diagnosed. She refused neck exploration.

Oral ergocalciferol was started at 50,000 IU/day and gradually increased to 200,000 IU/day. Bone pain persisted for several months but gradually decreased, while walking capacity and muscle power improved. Clinical calcium were raised while those of phosphate were low and of 25-hydroxy vitamin D normal. During vitamin D treatment plasma concentrations of calcium remained raised though those of parathyroid hormone fell to within the normal range. Alkaline phosphatase activity rose and then fell, while plasma phosphate concentrations rose and remained at the lower end of the normal range. Plasma 25-hydroxy vitamin D concentrations rose rapidly to a maximum of 425 nmol/l (170 ng/ml), when calcium absorption measured by a double isotope technique was 95%. Sequential bone biopsies showed a progressive reduction in the amount of osteoid, though this was never normalised. Plasma biochemistry became normal after parathyroidectomy and remained so. Postoperative maximum tubular reabsorption capacity for phosphate was 1.67 mmol/l (3.5 mg/100 mg) (normal 0.7-1.4 mmol/l; 2.2-4.3 mg/100 ml), indicating that renal phosphate handling was then normal.

Comment

This patient is unusual because she presented with severe osteomalacia, the hypercalcaemia being an unexpected observation. She

References


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was clearly not deficient in vitamin D, since her estimated vitamin D intake and plasma 25-hydroxy vitamin D concentrations were normal on admission. She responded slowly to vitamin D treatment both clinically and histologically despite supraphysiological plasma concentrations of 25-hydroxy vitamin D and high calcium absorption. The osteomalacia most probably resulted from chronic phosphate depletion secondary to long-standing hyperparathyroidism. Subsequently, the increased absorption of phosphate that results from vitamin D treatment would be countered by high urinary losses. Final correction of the problem was achieved only by parathyroidectomy. The fall in plasma parathyroid hormone concentrations observed during vitamin D treatment occurred without any consistent rise in plasma calcium and may reflect a direct action of a vitamin D metabolite on parathyroid function. It serves, however, to underline the complex interaction of these calcium-regulating hormones in normal and pathological conditions.

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Requests for reprints to Dr R R Ghose.

2 Dent CE, Jones EM, Mullan DP. Masked primary (or tertiary) hyperparathyroidism. Lancet 1975;i:1161-4.

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Treatment of unidentified viper bites

In the tropics many people die from snakebites, and all snakebites, although many produce no signs of systemic poisoning, must be considered as potentially life-threatening. Specific antivenom is effective treatment, but I believe that it is overused and too often given unnecessarily early. Most authorities suggest that antivenom should be used only when there are signs of systemic poisoning—e.g., cardiovascular or neurological disorders. Traditionally at this hospital patients bitten by snakes were seen by nurses and virtually all given subcutaneous antivenom automatically. We thought that most of these patients did not need antivenom, and so in August 1978 we introduced selective use of the antivenom, and I report our experience.

<table>
<thead>
<tr>
<th>Case No</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Local reaction to bite</th>
<th>Degree of bleeding</th>
<th>Result of clotting test</th>
<th>Dose of antivenom given before clotting test negative</th>
<th>Course and comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>40</td>
<td>F</td>
<td>Severe oedema of leg</td>
<td>Slight bleeding of gums</td>
<td>+</td>
<td>40 ml</td>
<td>Discharged after three days</td>
</tr>
<tr>
<td>2</td>
<td>26</td>
<td>M</td>
<td>Mild oedema of bitten foot</td>
<td>Bleeding of gums, slightly bloody sputum, and slight bleeding at the bite site after superficial incision</td>
<td>+</td>
<td>40 ml</td>
<td>Discharged after three days</td>
</tr>
<tr>
<td>3</td>
<td>20</td>
<td>M</td>
<td>Moderate oedema of leg</td>
<td>Severe bleeding from superficial incision on the head</td>
<td>+</td>
<td>60 ml</td>
<td>Discharged after three days</td>
</tr>
<tr>
<td>4</td>
<td>20</td>
<td>M</td>
<td>Moderate oedema of leg</td>
<td>Bleeding of gums and epistaxis</td>
<td>+</td>
<td>20 ml</td>
<td>Discharged after three days</td>
</tr>
</tbody>
</table>

Patients, methods, and results

Eighteen patients (16 males, 2 females, aged 12-45) presented between August 1978 and November 1979. All were questioned, examined, and had a test for clotting time using 2 ml of venous blood in dry, clean glass tubes. The test result was considered negative if the blood clotted within 10 minutes. All patients bitten within 12 hours of arrival at the hospital and all those with severe local reaction or signs of systemic poisoning were admitted and had their clotting time repeated after 4-6 and 24 hours. Those without signs of systemic poisoning were treated symptomatically and observed closely. Those with neurological disorders or clotting defects were given antivenom intravenously—20 ml Pasteur Institute’s anti-Bitis-Echis-Naja-serum in 1 litre of normal saline over 1-2 hours. If normal clotting was not re-established this was repeated.

All but one of the 18 had swelling around the site of the bite, which was always painful. (The remaining one had fang marks as evidence of a definite bite.) Some had enlarged tender lymph nodes, none had visible tissue necrosis, and in 17 the bite was on the leg (one had been bitten on the hand). The patients described the snake, but only one brought the dead snake with him. Patients arrived at the hospital between one hour and three days after the bite, and 11 had had some treatment before coming. The treatment given had no effect as far as we could tell in all but one case, where an incision made by a local healer had caused severe prolonged bleeding because of a clotting defect. Sixteen patients were admitted, none developed neurological disorders, four had clotting defects on arrival, and of the other 12 none displayed clotting defects. The four patients with clotting defects came to hospital more than 12 hours after being bitten (one three days after), but all eventually responded well to treatment (details in table). The other 12 were discharged without developing any complications.

Comment

We may reasonably assume that these patients were bitten by vipers, and we have shown that most patients coming to our hospital do not need antivenom. The selective use of antivenom not only reduces costs but also protects patients from the known hazards of giving heterologous serum. I emphasise, however, that those not given antivenom must be carefully observed as clotting defects can develop as late as 27 hours after the bite.

The Pasteur Institute does not recommend intravenous use of its anti-Bitis-Echis-Naja-serum, but we have had no problems using it intravenously. Nevertheless, should the amount of physiological saline as diluted be required in patients at risk of congestive cardiac failure? The advantages of intravenous infusion are that it offers better control and may be quickly discontinued if problems develop, that an intravenous line is to hand for any emergency treatment of anaphylaxis, and that an intramuscular haematoma is avoided.


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