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Parathyroid crisis and acute viral hepatitis B infection

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Summary: The simultaneous development of acute hyperparathyroidism and viral hepatitis B infection in a 72 year old male is described. Resolution of the hepatitis was accompanied by improvement in the parathyroid hormone mediated hypercalcaemia. It is postulated that antibodies to the hepatitis B virus may have altered the calcium 'set point' allowing uncontrolled synthesis and release of parathyroid hormone during the acute illness.

Introduction

Hypercalcaemia, a rarely recognized complication of acute viral hepatitis has been reported in association with acute non-A non-B hepatitis and attributed to virus-induced cytokine production.¹ Acute primary hyperparathyroidism (parathyroid crisis) has been described as an unusual form of hyperparathyroidism characterized by life-threatening hypercalcaemia² and has not previously been reported in association with viral hepatitis.

Case report

A 71 year old man was admitted with a 3 week history of anorexia, nausea, vomiting, malaise,

fatigue, arthralgia, myalgia and polyuria. A benign gastric ulcer and reflux oesophagitis, confirmed endoscopically, had been diagnosed 9 months previously and successfully treated with ranitidine 150 mg twice daily for 8 weeks. There was no history of transfusion with blood or blood products, homosexual contact, alcohol abuse, hepatotoxic drug ingestion, recent foreign travel, ingestion of antacids, lithium, thiazides, vitamin D or calcium-containing preparations. At presentation physical examination revealed jaundice and hepatomegaly in the absence of stigmata of chronic liver disease.

Results

Investigations revealed a serum albumin of 33 g/l (normal range: 35–50), bilirubin 85 mmol/l

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(4–17), aspartate transaminase 580 IU/l (8–40), alanine transaminase 700 IU/l (5–42), alkaline phosphatase 109 IU/l (30–110) and gamma glutamyl transferase 143 IU/l (0–50) as determined by standard laboratory techniques. Serological analysis revealed hepatitis B surface (HBs) and e (HBe) antigens (Abbott, UK) and antibodies to IgM HBe (HB core) (Amersham International, UK). Primary hyperparathyroidism was diagnosed on the basis of a raised serum intact parathyroid hormone (PTH) of 16.1 pmol/l (0.2–5.5; Allegro PTH, Nichols Institute) and a raised serum ionized calcium 1.62 mmol/l (1.19–1.33; analyte+2, Baker). Parathyroid function tests performed during the acute hepatitis B infection and 6 months later are shown in Table I. Serum 25-OH vitamin D was less than 5 nmol/l (14–79) and serum 1,25 (OH)₂ vitamin D was 69 pmol/l (38–144). Renal function was normal with a serum creatinine of 0.11 mmol/l (0.06–0.115) and a creatinine clearance of 75 ml/minute. Thyroid stimulating hormone was 1.4 mU/ml (0.15–3.2). There was no evidence of ectopic calcification, hyperparathyroid or metastatic bone disease on skeletal survey. Chest X-ray was normal. Leucocyte and red cell count was normal and erythrocyte sedimentation rate was 8 mm/hour.

Subsequent course

Treatment was commenced with intravenous saline infusions which were continuously required over a 3 week period to prevent life-threatening hypercalcaemia. With resolution of the clinical and biochemical features of acute hepatitis, the serum calcium returned towards normal (Figure 1). Re-evaluation at 6 months confirmed a diagnosis of primary hyperparathyroidism with a mildly elevated serum ionized calcium and an inappropriately ‘normal’ serum parathyroid hormone level (Table I).

Figure 1 Serum ionized calcium and ALT levels during the course of acute hepatitis B infection. –○– = ALT (IU/l); –●– = serum ionized calcium (mmol/l).

Discussion

The results indicate the simultaneous development of hepatitis B viral infection and acute hyperparathyroidism. The liver plays an important role in the metabolism of PTH, cleaving PTH (1–84) into N-terminal PTH (1–34) and biologically inactive C-terminal peptide.³ Both N-terminal and whole hormone PTH (1–84) are biologically active as the structural requirement for activity resides in the first 34 amino acids. There is, therefore, no requirement for cleavage of whole hormone for biological activity to be expressed. The kidneys also convert intact hormone to PTH (1–34) and C-terminal peptide. It is unlikely, therefore, that decreased liver catabolism of PTH (1–84) is responsible for the hypercalcaemia in this patient as increased renal metabolism may compensate for any excess circulating PTH arising as a result of severe hepatocellular necrosis.

Raised liver enzymes in a patient with subacute thyroiditis has been reported,⁴ liver enzymes returning to normal in association with resolution of the thyroiditis. Viral thyroiditis may result from

Table I Metabolic indices during and 6 months after acute hepatitis B viral infection

	Reference range	At presentation	At 6 months
Total calcium (mmol/l)	2.25–2.65	3.67	2.79
Ionized calcium (mmol/l)	1.19–1.33	1.72	1.36
Phosphate (mmol/l)	0.8–1.4	0.72	0.96
Serum PTH (pmol/l)	0.2–5.5	16.1	4.7
Urinary CAMP (nmol/l)	12.8–38.8	75.8	31.9
Nephrogenous CAMP (nmol/l)	0–26	47.5	16.7
TmPO ₄ /GF (mmol/l)	0.81–1.39	0.37	1.57
Serum 25(OH)D (mmol/l)	Feb/March 14–79	< 5	
	Aug/Sept 36–90		63.3
Serum 1,25(OH) ₂ D (pmol/l)	38–144	69	

release of a significant quantity of stored thyroid hormone. Stores of PTH are limited in comparison with those of other endocrine glands, and are only sufficient to meet basal secretory needs for approximately 6 hours.⁵ Under conditions of maximal stimulation, PTH stores become exhausted after only 1½ hours without an increased rate of hormone synthesis. The sudden release of stored PTH would not cause an aggressive hypercalcaemic phase of 6 weeks duration as was evident in this case.

PTH enhances the activity of the 1- α -hydroxylase enzyme responsible for the conversion of 25 (OH) vitamin D to 1,25 (OH)₂ vitamin D. The normal 1,25 (OH)₂ vitamin D reported in this patient despite the stimulus of a high circulating PTH may have resulted from lack of precursor 25 (OH) vitamin D during the acute phase of the illness. It may have also contributed to the raised PTH and concomitant hypercalcaemia by not exerting the normal feedback control on PTH synthesis. The hypovitaminosis D recorded initially was more likely to be due to a deficiency state⁶ rather than as a result of hepatitis, as 25-hydroxylation can be maintained in the presence of significant liver disease.⁷

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