Hypercalcaemia

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A 48-year-old woman with a previous history of Graves' disease presented to the Accident and Emergency department with a short history of nausea, vomiting and abdominal pain. On examination she was thin, clinically dehydrated and had bilateral proptosis with a moderately sized diffuse goitre. Abnormal biochemical investigations are shown in line (a) in the table. The following investigations were normal: plasma urea and creatinine, chest X-ray, serum angiotensin-converting enzyme, plasma protein electrophoresis and serum 1,25 (OH)₂ vitamin D. She was treated with intravenous rehydration and pamidronate infusion. Carbimazole therapy was commenced and she was rendered euthyroid. Subsequent serum calcium and parathyroid hormone levels are shown in line (b) in the table. Carbimazole was later withdrawn in preparation for radioactive iodine therapy following which she became clinically thyrotoxic with calcium and parathyroid hormone concentrations as shown in line (c) in the table. At this time an exacerbation of dysthyroid eye disease necessitated treatment with oral steroids (prednisolone, 30 mg daily) which did not affect serum calcium concentrations over a two-week period. Following radioactive iodine therapy she has remained euthyroid with a mean serum calcium concentration of 2.7 mmol/l.

Table Biochemical investigations (for explanation, see text)

	Calcium (mmol/l)	Intact parathyroid hormone (pg/ml)	Phosphate (mmol/l)	Free thyroxine (pmol/l)	Thyroid- stimulating hormone (mU/l)	Thyroid peroxidase antibodies
Normal range	2.1–2.6	10–65	0.8–1.5	9–25	0.4–4.0	
(a)	3.7	30.5	0.88	>127	<0.01	1:6400
(b)	2.57	69.0		14.4	0.01	
(c)	3.27	10.5		48.0	<0.01	

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Questions

- 1 What are the initial two diagnoses?
- 2 Explain the changes in serum calcium and parathyroid hormone concentrations shown in the table.

Answers

QUESTION 1

Graves' disease and primary hyperparathyroidism

QUESTION 2

During periods of thyrotoxicosis, hypercalcaemia is exacerbated resulting in negative feedback effects on parathyroid hormone secretion. During euthyroidism these effects are reversed, allowing parathyroid hormone secretion to increase.

Comment

Thyrotoxicosis associated with primary hyperparathyroidism results in a complex disturbance of calcium homeostasis. Hypercalcaemia due to osteoclast-mediated bone resorption occurs in 2–5% of patients with thyrotoxicosis¹ and is usually asymptomatic, normalising completely when euthyroidism is restored.^{1,2} Associated primary hyperparathyroidism accounts for less than 1% of these cases and should only be diagnosed when the patient is euthyroid as parathyroid hormone secretion may be stimulated by thyroid-hormone-mediated catecholamine release.⁴ Fluctuating serum calcium and parathyroid hormone levels corresponding to changes in thyroid function may be due to suppression of parathyroid hormone secretion by thyrotoxicosis-mediated hypercalcaemia, effects which are reversed when euthyroidism is restored. Phosphate concentrations may be unchanged due to the opposing effects of thyrotoxicosis and hyperparathyroidism.^{4,5}

Coexisting thyrotoxicosis and primary hyperparathyroidism may cause diagnostic difficulties. Hypercalcaemia should not be assumed to be secondary to thyrotoxicosis,

Learning points

- hypercalcaemia associated with thyrotoxicosis is usually mild, asymptomatic and reversible
- persistently elevated serum calcium in a treated thyrotoxic patient should prompt a search for other causes of hypercalcaemia
- secretion of parathyroid hormone may be stimulated by thyroid-hormone-mediated catecholamine release; primary hyperparathyroidism should only be diagnosed when hypercalcaemia persists despite normalisation of thyroid function
- calcium feedback control of parathyroid hormone secretion may persist in primary hyperparathyroidism

particularly when the serum calcium level is markedly elevated and does not fully normalise when euthyroidism is achieved. The persistent modulatory effect of serum calcium on parathyroid hormone in primary hyperparathyroidism must be considered when making the diagnosis. The combined effects of the two conditions on bone density measurements is of importance and remains to be clarified.

Final diagnosis

Coexistent Graves' disease and primary hyperparathyroidism.

Keywords: Graves' disease, hypercalcaemia, primary hyperparathyroidism

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