

Hyperthyroidism, an overlooked cause of severe hypercalcaemia

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Abstract

We present a case of severe symptomatic hypercalcaemia secondary to hyperthyroidism alone. Hypercalcaemia was managed with pamidronate which unfortunately resulted in transient hypocalcaemia. The key message is that thyroid function should be checked in all patients who present with hypercalcaemia and that endocrine input is needed sooner rather than later for appropriate management.

Keywords

Hypercalcaemia; thyrotoxicosis.

Introduction

Hypercalcaemia is infrequently associated with thyroid disease, and in most cases is mild with the adjusted calcium <3.00 mmol/L. In thyrotoxic hypercalcaemia, possible symptoms of hypercalcaemia may mask those of hyperthyroidism. We present this rather unusual case and describe the effect of thyroid hormone on calcium metabolism.

Case report

A 22-year-old woman first presented with headache, nausea, neck stiffness, photophobia and anxiety. Lumbar puncture ruled out viral meningitis and a diagnosis of viral illness was made. Her electrolytes and calcium levels at this stage were all within the normal range and she was discharged. Three weeks later she was again admitted with a history of vomiting and abdominal pain. On discussion it was noted that the symptoms had been present for the past 4 weeks, during which she had significant weight loss and complained of generalised weakness and long-standing menstrual irregularities. On examination she had a non-tender palpable goitre with a bruit, hand tremor and sweaty palms and her electrocardiogram (ECG) showed sinus tachycardia. Her electrolytes were within the normal range, however her adjusted serum calcium was 3.15 mmol/L and she was hyperthyroid, with a suppressed thyroid-stimulating hormone (TSH) level of <0.05 mIU/L, free T4 of 100.0 pmol/L and free T3 of >30 pmol/L (normal ranges TSH,

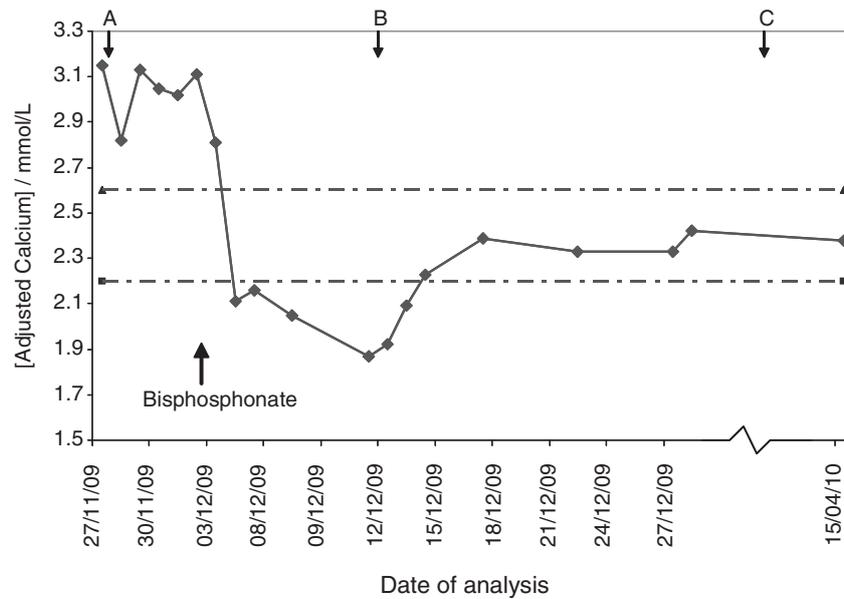


Fig. 1. Level of adjusted calcium after treatment for thyrotoxicosis. The level of albumin adjusted calcium is shown (solid line), along with the upper and lower reference limits (dashed lines). The point at which bisphosphonate was administered is also indicated. The levels of thyroid hormones for the points marked on the graph are as follows: (A) TSH <0.05 mIU/L, free T4 >100 pmol/L, free T3 >30 pmol/L; (B) TSH <0.05 mIU/L, free T4 25.7 pmol/L, free T3 6.9 pmol/L; (C) TSH 0.24 mIU/L, free T4 10.2 pmol/L, free T3 2.6 pmol/L.

0.3–5.5 mIU/L; free T4, 12–22 pmol/L; free T3, 3.1–6.8 pmol/L). Her renal function remained normal, with estimated glomerular filtration rate (eGFR) >60 mL/min.

Other causes of hypercalcaemia were excluded as parathyroid hormone (PTH) was appropriately suppressed (5 ng/L; normal range 15–65 ng/L), vitamin D was 35 nmol/L (<50 nmol/L insufficient and <25 nmol/L deficient). An ultrasound scan of the abdomen and chest radiograph showed no detectable abnormalities that could cause hypercalcaemia. Basic biochemistry also did not point to any underlying malignancy that could cause hypercalcaemia (lactate dehydrogenase (LDH), protein electrophoresis, immunoglobulins and serum free light chains were all normal). There was no radiographic evidence of sarcoidosis disease, plus her angiotensin-converting enzyme levels were also normal. There was no other evidence of granulomatous disease or any previous history of excessive antacid use.

Thyroid antibody levels were raised at 218 kU/L (normal levels 0–34 kU/L), supporting a diagnosis of autoimmune hyperthyroidism. She was started on carbimazole (20 mg twice daily), along with propranolol (40 mg three times daily) in view of sinus tachycardia. Her calcium level remained high (>2.90 mmol/L) despite intravenous fluids and she was given pamidronate infusion on day 5 after admission by the on-call team. Over the next few days she became hypocalcaemic with a lowest adjusted calcium value of 1.77 mmol/L, which had to be corrected with calcium supplements. She developed a rash due to carbimazole and hence had to be switched to propylthiouracil. She subsequently had radioactive iodine and remains euthyroid. Her serum calcium level is also normal (Fig. 1).

Discussion

Hypercalcaemia due to hyperthyroidism is well documented, but the mechanism for the hypercalcaemia is incompletely understood. There is modification of the bone remodelling cycle in hyperthyroidism^[1]. T3 is thought to stimulate osteoclast differentiation, which leads to accelerated bone resorption relative to bone mineralization^[2]. Our case is unusual as our patient had significant hypercalcaemia secondary to hyperthyroidism alone (3.15 mmol/L) compared with mean values ranging from 2.53 to 2.70 mmol/L in other reported series^[3,4]. The resulting hypercalcaemia consequently suppressed the levels of serum parathyroid hormone and 1,25-dihydroxyvitamin D, and intestinal absorption of calcium is reduced in these patients. This process can result in osteoporosis associated with hyperthyroidism over a long period of time^[5].

In severe thyrotoxicosis, as is presented here, vomiting can amplify the degree of hypercalcaemia through dehydration. Increased levels of calcium act to increase osmotic diuresis, further exacerbating the situation and so it is essential that the cause of hypercalcaemia is correctly identified. In thyrotoxic hypercalcaemia the symptoms of hypercalcaemia, such as nausea, vomiting and abdominal pain, may predominate and mask the symptoms of thyrotoxicosis, risking the development of thyrotoxic storm due to a delay in diagnosis if hyperthyroidism is not considered promptly^[6]. After diagnosis, it is important that the patient is carefully managed with fluid treatment to avoid unnecessary complications; for example, avoidance of bisphosphonates which induced hypocalcaemia in this patient.

Conclusion

This case highlights the need to consider hyperthyroidism as a cause of hypercalcaemia, even at pronounced levels of calcium and careful consideration has to be given prior to pamidronate administration to ensure the risk of hypocalcaemia and electrolyte abnormalities are minimised.

Teaching points

- Hypercalcaemia in thyroid disease occurs infrequently, but should always be considered as a cause, even if thyroid function tests have been normal in the previous few months.
- Routine plasma calcium estimations should be performed in all cases of hyperthyroidism.
- Fluid treatment is essential in patient management and can be used while awaiting PTH results and endocrine input, potentially avoiding the use of a bisphosphonate.
- Symptomatic hypercalcaemia is an unusual presentation of hyperthyroidism that resolves once the hyperthyroidism has been treated.
- Exclusion of malignancy is always important in the differential diagnosis of hypercalcaemia with suppressed PTH.

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