

Severe hypercalcaemia following vitamin D replacement therapy in a patient found to have co-existing sarcoidosis and primary hyperparathyroidism

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Introduction

Current guidance recommends replacing vitamin D in patients with mild primary hyperparathyroidism although there are reports of worsening hypercalcaemia in some patients. Vitamin D replacement has also been known to cause hypercalcaemia in patients with sarcoidosis. We present a case of a patient with co-existent sarcoidosis and primary hyperparathyroidism, who developed severe hypercalcaemia following treatment with high dose vitamin D.

Case Report

A 63 year old woman presented to hospital with symptomatic hypercalcaemia (nausea, vomiting, anorexia and general malaise.) Her admission calcium levels were 3.59mmol/l, with mild acute renal impairment (creatinine 132umol/l, estimated glomerular filtration rate 37ml/min). Parathyroid hormone (PTH) level was 2.0pmol/l (PTH reference range 1.0-6.1 pmol/l)

Her past medical history included pulmonary hypertension secondary to chronic venous thromboembolism. Two months previously she sustained a fractured neck of femur and found to have low levels of vitamin D (<12.5nmol/l.) She was treated with high dose vitamin D replacement (60,000 units colecalciferol for five days total) followed by maintenance therapy (1600 units colecalciferol once daily.)

The onset of her presenting symptoms coincided with initiation of this therapy. Serology prior to this treatment had shown a calcium level of 2.73 mmol/l, coincidental with a PTH of 10.6pmol/l.

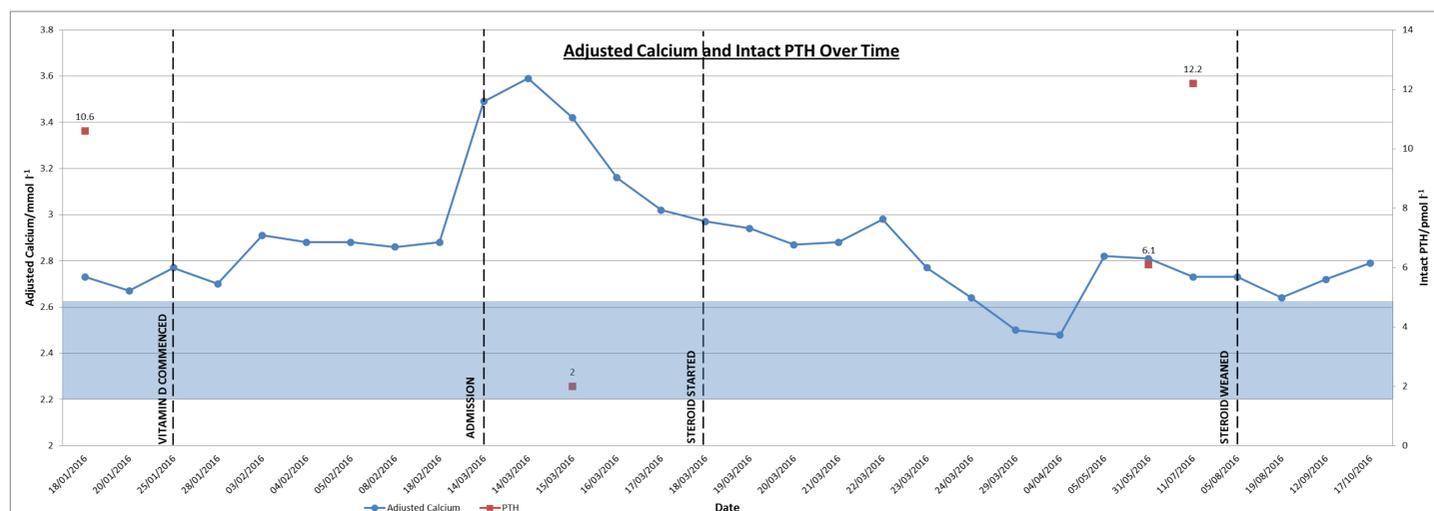
She was initially managed with intravenous rehydration as well as pamidronate therapy, however neither therapy effectively reduced serum calcium levels which remained above 3 mmol/l.

A CT scan was then obtained, which demonstrated mediastinal and abdominal lymphadenopathy, unchanged in appearance from a CT scan one year prior. Subsequent review of her medical notes found that following this scan, a lymph node biopsy had been performed which had shown features of sarcoidosis. The medical team who initiated Vitamin D replacement were unaware of this result.

Steroid treatment (prednisolone, 30mg once daily) was commenced for sarcoid-associated hypercalcaemia and calcium levels returned to normal within 5 days of this. A trial without steroid treatment has been unsuccessful with subsequent rise in calcium levels again.

A MIBI scan was also obtained, and demonstrated a likely parathyroid adenoma. There was biochemical evidence of primary hyperparathyroidism from 3 years prior to this admission, suggesting she had co-existing primary hyperparathyroidism and sarcoidosis.

Results & Clinical Timeline



Discussion and Conclusions

Vitamin D deficiency is more common in patients with primary hyperparathyroidism (PHPT) compared with the general population and is often associated with an aggravated form of disease.

The mechanism for this is not clear and could be due to increased conversion of 25-(OH)D to 1,25-(OH)₂ and enhanced degradation of Vitamin D.

Vitamin D deficiency in PHPT is associated with:

- higher pre-operative PTH levels
- increased adenoma weight
- more severe bone disease
- Higher risk of post-op hypocalcaemia
- Persistent post-op elevated PTH levels
- Increased CV mortality

The diagnosis of PHPT can be obscured by concomitant Vitamin D insufficiency.

Replacing Vitamin D improves diagnostic separation of PHPT and secondary hyperparathyroidism; as well as lowering PTH and bone turn over pre-op to reduce risk of post op hypocalcaemia. Evidence is not clear on the long term benefit of replacing Vitamin D in patients with mild PHPT not undergoing surgery.

There are reported cases of hypercalcaemia worsening after Vitamin D replacement in PHPT but in general evidence suggests that it is safe to do so in patients with mild PHPT providing calcium levels are monitored due to the small risk of increasing calcium levels with treatment.

10-20% of patients with sarcoidosis will present with hypercalcaemia due to tissue level conversion of 25-(OH)D to 1,25-(OH)₂ by sarcoid granulomas.

There is no clear evidence regarding the use of Vitamin D replacement in sarcoidosis and most guidelines advise to do so with caution and not to routinely supplement with Vitamin D, but to use alternatives such as bisphosphonates.

Sarcoid associated hypercalcaemia is steroid responsive.

References

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