

# Unmasking normocalcaemic hyperparathyroidism (nPHPT) resulting in severe hypercalcaemia from lack of monitoring during in the COVID pandemic

## Abstract

Primary hyperparathyroidism (PHPT) is a common endocrine disorder in the older person although the incidence of normocalcaemic primary hyperparathyroidism (nPHPT) remains largely unknown. Whilst the majority of patients with PHPT asymptomatic, we describe a case of severe symptomatic hypercalcaemia from undiagnosed nPHPT whilst on calcium and vitamin D supplements. This is an important reminder to clinicians that serum calcium should be monitored before and after initiation of calcium and vitamin D supplementation in the older person.

**Keywords:** primary hyperparathyroidism, normocalcaemic primary hyperparathyroidism, calcium and vitamin d supplements, older people

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## Key points

Primary hyperparathyroidism is common in older people, and the majority are asymptomatic.

Raised calcium with a normal parathyroid hormone does not exclude primary hyperparathyroidism.

Serum parathyroid hormone is not routinely checked before initiating calcium and vitamin D in the older person.

It is important to check serum calcium before and after initiation of calcium and vitamin D supplements.

## Case report

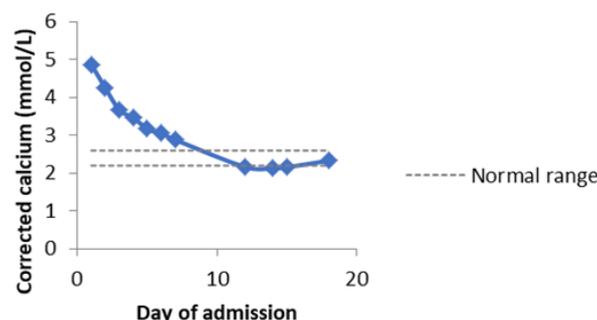
A 75-year-old lady presented with acute hypoactive delirium. She had a history of osteoporosis, falls, neck of femur fracture, breast cancer and chronic obstructive pulmonary disease. Her medications included calcium and vitamin D for secondary fracture prevention. She had annual blood test via her general practitioner. Her renal function serum calcium and vitamin D had been normal over the past two consecutive years, however she had missed her test in April 2020 due to COVID-19.

On admission she had an abbreviated mental test score (AMTS) of 4/10. Blood tests showed creatinine 325 μmol/L (44-80 μmol/L), urea 16.1 mmol/l (2.5 -7.8 mmol/l), corrected calcium of 4.87 mmol/L

(normal range 2.20 - 2.60 mmol/L), haemoglobin 112 g/L, WCC 13.6 x10<sup>9</sup>/L, neutrophils 11.0 x10<sup>9</sup>/L, CRP 57 mg/L. Sodium, potassium, and albumin were normal. Chest X-ray showed old rib fractures. Respiratory viral screen and COVID-19 swabs were negative. Renal ultra sound demonstrated no hydronephrosis. On the first day of admission, parathyroid hormone (PTH) was non-suppressed at 7.0 pmol/L (normal range 1.6-6.9 pmol/L). Following rehydration and bisphosphonate therapy, she developed a transient, asymptomatic hypocalcaemia and her PTH was elevated at 18.3 pmol/L on the 13<sup>th</sup> day of admission.

Investigations for hypercalcaemia excluded myeloma, sarcoidosis and hyperthyroidism. Her vitamin D was within the normal range. Her 24 hour urinary calcium: creatinine ratio was 0.021. Contrast CT of chest, abdomen and pelvis showed no recurrence of her previous malignancy.

Calcium and vitamin D supplements were stopped. She was treated with slow intravenous fluids, and subsequently intravenous pamidronate. She also received antibiotics to cover potential infective exacerbation of COPD. Over the course of her admission, her mental state improved and her AMTS was 10 out of 10. Her renal function and serum calcium also improved prior to hospital discharge (Figure 1). At four months post discharge, the patient has remained well with a normal serum calcium of 2.49 mmol/L and an elevated PTH 16.6 pmol/L.



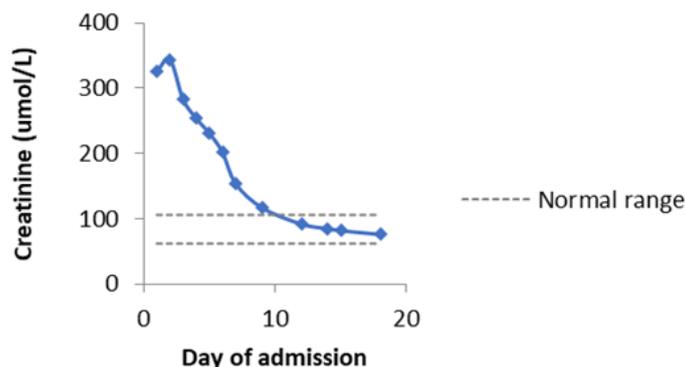


Figure 1 Graphs to show corrected calcium and creatinine levels during the patient’s admission.

## Discussion

Primary hyperparathyroidism (PHPT) is an endocrine disorder caused by overproduction of PTH, resulting in derangement of calcium metabolism. PHPT is more common in older women,<sup>1</sup> with 85% being asymptomatic.<sup>2</sup> Elevated serum calcium level with raised plasma PTH level points towards a diagnosis of PHPT. However, a single normal PTH result does not exclude PHPT, as PTH is released in a biphasic circadianrhythm.<sup>3</sup> However, incidence of nPHPT is largely unknown and possibly an early form of PHPT. Familial hypocalciuric

hypercalcaemia is a rare inherited condition due to a mutation of calcium-sensing receptor gene, where patients have hypercalcaemia and hypocalciuria with normal or elevated PTH. In our case, the calcium creatinine clearance ratio (Ca:Cr ratio) is suggestive of PHPT as it is above 0.01, whereas in FHH, Ca:Cr ratio is usually below 0.01. nPHPT is usually uncovered during a work up for osteoporosis where the serum calcium is normal and renal function and vitamin D but PTH is elevated. Table 1 summarizes the biochemical profile of the four types of hyperparathyroidism.

Table 1 Summary of types of hyperparathyroidism and biochemistry

Type	Serum calcium	Serum PTH	Vitamin D	Renal function
PHPT	raised	Raise or normal	normal	normal
nPHPT	normal	Raise	Normal	normal
Secondary hyperparathyroidism	Normal or reduced	Raise	Usually Low(look for other causes e.g medication)	Usually normal
Tertiary hyperparathyroidism	Raised	Raised	Normal or low	abnormal

Our patient had nPHPT. She was receiving calcium and vitamin D supplements and was unable to attend her yearly blood test due to COVID-19. Her PTH was not checked prior to commencement of calcium and vitamin D. nPHPT was unmasked and she presented with symptomatic hypercalcaemia requiring hospitalisation. She developed a transient hypocalcaemia following hydration and bisphosphonates. This is a well described phenomenon. Her transient low serum calcium resulted in feedback to raise PTH secretion, increasing resorption of calcium from bone, absorption from the GI tract and tubular reabsorption to normalise serum calcium.<sup>4</sup> Four months post discharge, her serum calcium remains normal and PTH remains elevated, further supporting a diagnosis of normocalcaemic PHPT.

The older person is more likely to be on calcium and vitamin D supplements, often initiated after assessment of falls. Often than not, PTH assay is not requested. For patients with PHPT and nPHPT who are osteoporotic and at risk of falls, they should receive vitamin D supplementation without calcium. As a safe guard, serum calcium should be monitored before and after initiation of calcium and vitamin D supplementation in the older person.

## Declaration of consent

Written consent for publication of clinical details was obtained from patient.

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## Availability of data and material

Not applicable.

## Code availability

Not applicable.

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## Conflicts of interest

The authors declare that there is no conflict of interest.

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