Establishing the diagnosis in an atypical case of primary hyperparathyroidism

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Case History:
A 62-year-old man was referred from secondary care with a long history of recurrent ureteric colic, borderline hypercalcaemia with parathyroid hormone level in the low–normal range and a normal serum phosphate. There was no family history of kidney stones or osteoporosis and no history of childhood urinary infections.

Investigations and Method:
Repeated biochemistry at presentation was as follows: PTH 2.1 pmol/l (1.1–6.8), corrected calcium 2.56 mmol/l (2.15–2.55), phosphate 1.10 mmol/l (0.8–1.40) and 25 OH vitamin D 48 nmol/l (25–100). A 24 hour urine collection of 6.9 litres contained an elevated total calcium of 12.01 mmol. A myeloma screen was negative and serum ACE was within the normal range. Renal stone analysis on 3 occasions demonstrated 100% calcium phosphate stones. The differential diagnosis at this stage was 1) Atypical hyperparathyroidism, 2) Idiopathic hypercalciuria with stone formation, 3) Partial distal renal tubular acidosis 4) Other causes e.g. elevated activated vitamin D or a circulating PTH related peptide.

Results and Treatment:
An ammonium chloride load test excluded partial distal renal tubular acidosis. Urine excretion of urate, oxalate, Mg and citrate was within normal limits. PTH rP was <0.7 pmol/L and 1,25-OH vitamin D was also normal at 0.49 pgm/L. A CT urogram revealed ongoing stone formation with evidence of 4 separate calcific densities within the urinary tract. In order to reduce the hypercalciuria, a thiazide diuretic was prescribed and this produced a sustained elevation in plasma calcium (2.69–2.82 mmol/l). Primary hyperparathyroidism was now strongly suspected and localisation studies were pursued.

Ultrasound of the neck showed a possible left superior parathyroid adenoma and sestamibi was unsurprisingly negative. An MDT discussion based on the options of surgery or watchful waiting fell temporarily in favour of the latter. However several months later urinary calcium remained high despite thiazide therapy and cinacalcet was able to suppress the plasma calcium to the lower half of the normal range (2.17 mmol/l), suggesting a relatively large parathyroid component to the hypercalcaemia. A DEXA scan also demonstrated lumbar osteopaenia.

Conclusion:
The patient went on to have an uncomplicated 4 gland exploration of the parathyroids. The left superior parathyroid gland appeared abnormal to the naked eye and reported histologically as a parathyroid adenoma confirming our original diagnosis.

Points for Discussion:
Why was the PTH in the lower–normal range?
Renal stone composition in primary hyperparathyroidism.
Comments on our differential diagnosis.
Cinacalet acting as a form of suppression test and thiazide therapy as a form of stimulation.