

## CLINICAL VIGNETTE

# Primary Hyperparathyroid Disease Presenting as Osteopenia

Matteo Dinolfo, M.D., and Jeffrey S. Goldsmith, M.D.

An otherwise healthy 57-year-old post-menopausal female presented to establish primary care. As part of her evaluation, a bone mineral density exam was obtained that showed low bone mass with a T score of -2.0. Subsequent Parathyroid studies showed an elevated PTH level in the context of normal Vitamin D levels, as well as an elevated 1-25 Di OH level. A 24-hour urine calcium/creatinine collection showed a ratio supportive of primary hyperparathyroidism.

Ultrasound of the thyroid and parathyroid glands showed a small hypoechoic nodule in the inferior right thyroid lobe. It was deemed a candidate parathyroid adenoma. A follow-up radionuclide parathyroid study showed this same region having persistent tracer uptake, consistent with a parathyroid adenoma. She underwent total parathyroidectomy with auto transplant as all four glands were grossly abnormal. Pathology showed hyper-cellularity in all four glands. Two months post-operatively, the patient did present to the Emergency Room with a 5 mm right UVJ stone causing mild right-sided hydronephrosis. She was able to pass this with conservative medical therapy, and follow-up CT scanning showed no residual nephrolithiasis. At one-year follow up, the patient remained asymptomatic with normal PTH levels and normal calcium levels.

### Discussion

Primary hyperparathyroidism (PHPT) is the most common cause of hypercalcemia. Diagnosis is usually made initially with serum calcium and confirmed with elevated intact parathyroid level or inappropriate high normal level given patients elevated calcium. All secondary causes of hyperparathyroidism should be ruled out and ionized calcium may be normal. Normal calcium hyperparathyroidism was first discovered in 2009.<sup>1</sup> The patient is usually diagnosed in the setting of low bone density. PTH levels are elevated in the absence of hypercalcemia.<sup>2,3</sup>

Secondary causes of hyperparathyroidism must be ruled out and ionized calcium should be normal. Previous calcium levels should be reviewed.<sup>4</sup> PTH should be measured with same serum sample as serum calcium.<sup>5</sup> Approximately 80-90 percent of patients with PHPT have elevated PTH level.<sup>6,7</sup> 10-20 percent have normal PTH levels but are inappropriate in the presence of elevated calcium.

Patients with non-parathyroid hypercalcemia have PTH level below 20-25 pg/dL. 24-hour urine calcium excretion may help

differentiate PHPT from Familial Hyperparathyroidism.<sup>8,9</sup> Low PTH levels would indicate non PTH mediated hypercalcemia. Approximately 40 % of patients have hypercalcemia.<sup>7</sup> Calcium excretion less than 200mg/day would indicate FHH or PHPTH with decrease Vitamin D.<sup>10</sup>

Low urinary calcium can occur in patients with low calcium intake. An elevated urinary calcium greater than 200-300mg/day rules out Familial hypocalciuric hypercalcemia (FHH). A calcium/Creatinine clearance rate which is the fractional excretion of calcium is also helpful. A value below 0.01 in Vitamin D replete patient is suggestive of FHH rather than PHPT where ratio is usually greater than 0.02.<sup>11-13</sup>

Differentiation of secondary Hyperparathyroidism due to Vitamin D deficiency from normocalcemic PHPT in patients with elevated PTH and normal serum calcium. Measure 25(OH) D, which is low in former and normal in latter. Elevations in PTH in individuals with PHPT cause greater conversion of 25-hydroxyvitamin D (25[OH]D; calcidiol) to 1,25 dihydroxyvitamin D (calcitriol) and therefore result in an elevation in calcitriol.<sup>14-16</sup>

### Differential Diagnosis/ Conclusion

The most common presentation of PHPT is asymptomatic hypercalcemia with elevated or high normal intact PTH. Laboratory testing can often distinguish FHH and secondary hyperparathyroidism. Malignancy and PHPT account for the majority of cases.

Malignancy is usually evident by the time hypercalcemia is noted. Calcium levels tend to be higher in malignancy and patients are more symptomatic than in PHPT. In atypical presentations such as occult malignancy or in some cases of severe hypercalcemia in PHPT. Levels of intact PTH are usually low or undetected in malignancy and elevated or high in PHPT. Rarely PTH secreting tumors add difficulty in arriving at a diagnosis.

Familial Hypocalciuric Hypercalcemia is characterized by low urinary calcium and normal PTH levels. FH in young children without symptoms should alert a physician to the diagnosis. 20% of patients with FHH have mildly elevated PTH levels. It is important to distinguish since FHH is a benign inherited disorder that does not require parathyroidectomy.<sup>11,12,17,18</sup>

The major distinguishing feature is low urinary calcium and low calcium/Cr clearance ratio. In absence of Vitamin D deficiency, most patients with OHOT have normal or elevated urinary calcium excretion.<sup>11,12,17</sup>

Drugs that affect calcium metabolism should also be considered. Thiazide diuretics reduce urinary calcium excretion and can cause mild hypercalcemia. Lithium decreases parathyroid sensitivity to calcium and may also decrease urinary excretion of calcium. Drugs should be withdrawn if possible and recheck calcium and PTH levels in 3 months.

Secondary hyperparathyroidism occurs with decreased renal function and impaired Vitamin D<sub>1,25</sub>OH production as well as patients with low dietary calcium intake or malabsorption.

Workup should include urinary calcium excretion, serum 25 OH Vitamin D, Bone density, and serum calcium/creatinine clearance. If urinary calcium is greater than 400mg/day surgical intervention is recommended. If Vitamin D is low, the Vitamin D should be repleted.

Patients with subclinical nephrocalcinosis or calcium renal stones with symptomatic disease would be candidates for surgical intervention. The degree of bone loss on DEXA is indicative of severity of hyperparathyroidism. Parathyroid scan can often reveal solitary adenoma as was evident in this patient.

In the case described, the patient was asymptomatic upon presentation. She was found to have osteopenia and primary hyperparathyroidism. The elevation in PTH resulted in higher Vitamin D<sub>1,25</sub>OH levels noted. The definitive treatment is surgical removal and was therefore indicated.<sup>19</sup> It is assumed that her nephrolithiasis was associated with her condition and definitive surgery should reduce risk of recurrent stone formation.

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