CASE REPORT

Prolonged Primary Hyperparathyroidism: Are We Overtreating our Patients?

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Abstract

Primary Hyperparathyroidism is increasing in incidence likely due to enhanced screening and diagnostic methods. Current recommendations encourage surgical management for patients who are symptomatic or who have evidence of organ involvement. However, in some cases who have had long-standing disease with minimal impact, a more conservative approach may be prudent. This case report presents a 68-year-old retired physician with type 2 diabetes managed in the Endocrinology clinic, incidentally discovered to have long-standing primary hyperparathyroidism (PHPT) during routine lab investigations. Despite a history of recurrent kidney stones and elevated parathyroid hormone (PTH) levels over 40 years, the patient remains relatively asymptomatic with minimal end-organ involvement. Current diagnostic and therapeutic recommendations suggest surgical intervention; however, the patient, given his lengthy disease course, opts for a conservative approach. This case prompts a reconsideration of individualized management strategies in the era of precision medicine.

Keywords

Hypercalcemia, Recurrent kidney stones, Parathyroid hormone, Osteoporosis, Type 2 diabetes, Endocrinology

INTRODUCTION

Primary hyperparathyroidism (PHPT) is a condition characterized by elevated serum calcium levels due to excess parathyroid hormone secretion. The most recent recommendations published after 2014 include Guidelines for the Management of Asymptomatic Primary Hyperparathyroidism: Summary Statement from the 4th International Workshop published in JCEM 2014, Primary Hyperparathyroidism: review and Recommendations on evaluation, diagnosis, and management, a Canadian and international consensus published in Osteoporosis International in 2017, hyperparathyroidism (primary): diagnosis, assessment and initial management published by the National Institute of health and care excellence in 2019 as well as evaluation and management of primary hyperparathyroidism: summary statement and guidelines from the 5th international workshop published in JBMR in August of 2022. The latter, most recent guidelines recommend that individuals with elevated serum calcium adjusted for albumin with elevated or inappropriately normal intact parathyroid hormone on two occasions at least two weeks apart is diagnostic for hypercalcemic primary hyperparathyroidism (Bilezikian, 2022). This case explores a patient with a long-standing PHPT and the challenges of reconciling historical management norms with evolving contemporary approaches, emphasizing the importance of personalized care.

CASE PRESENTATION

This is a 68-year-old retired physician presenting to the Endocrinology clinic for the management of type 2 diabetes. During the visit, a review of his recent lab investigations incidentally revealed a mildly elevated calcium level of 11 mg/dl. His past medical history was significant for type 2 diabetes, dyslipidemia, ischemic heart disease post-stenting several years ago, hypothyroidism, and a previous history of kidney stones. On further history taking, it was revealed that he had a remote history of over 40 years ago of multiple kidney stones; he reported that his first kidney stone occurred in 1981, followed by multiple kidney stones every few years after that, with the last documented kidney stone in 2014. He was also told at that time that he had elevated PTH and questionable parathyroid hyperplasia which was never further followed up or investigated as he was unwilling to undergo a Sestamibi scan at the time of the discussion. He also reports a history of low bone density diagnosed several years ago which was not followed up or treated since then. He was offered treatment with cinacalcet, which he declined. His current medications include dulaglutide, insulin degludec, metformin, empagliflozin, Gliclazide MR, rosuvastatin, valsartan, bisoprolol, clopidogrel, pantoprazole 40 mg BID, vit D 5,000 IU daily, vitamin B12, and thyroxine. He has no known allergies, is a non-smoker, and reports no family members with a similar history of kidney stones. Further review of his current lab investigations revealed mildly decreased calculated EGFR at 72 µmol/ml. As he continues to refuse nuclear imaging at this time, we proceeded with a neck ultrasound and a follow-up DEXA scan to evaluate his bone density.

Current recommendations for the diagnosis and management of hyperparathyroidism suggest that for initial investigations, serum calcium should be measured as well as vitamin D levels, PTH level, 24-hour urine calcium, or urine calcium to creatinine ratio. Additionally, it is important to assess for possible end-organ damage resulting from hypercalcemia. As this case occurred over 40 years ago, not all these investigation results are available to me when writing this case report. Available relevant laboratory investigations grouped by date were as follows:

- 2008: 25(OH) Vitamin D 17.05 nmol/L, TSH 6.7 mIU/L, Serum Calcium 10.98 mg/dl, Serum Phosphorous 1.07 mmol/L.
- 2015: PTH 3.28 pmol/L, 25(OH) Vitamin D 45.39 nmol/L, Serum Calcium 10.82 mg/dl, Serum Phosphorous 1.06 mmol/L, Serum magnesium 1.48 mg/dl, Alk phosphatase 31 U/L, Albumin 4.5 g/dl, 24 hr urine calcium 8.04 mmol/24 hrs, 24 hr urine oxalate 31.25 mg/24 hrs.
- Investigations done in a different facility (Figure 1)

Thyroid Ultrasound in 2007 and repeated in 2024 did not show any parathyroid adenomata or hyperplasia. A DEXA scan in 2015 (Figure 2).

Repeat investigations at the time of writing this report showed the following results: PTH 11.04 pmol/L (normal range 1.59-7.24), creatinine 117 µmol/L (62-115 µmol/L), calcium 2.54 mmol/L (2.08-2.65 mmol/L), serum phosphate 0.7 mmol/L (0.78-1.65 mmol/L).

Repeated BMD in 2024 was reported as shown in Figure 3.

Accumulative Results

Creatinine

03/03/21	01/10/18	29/09/18	20/09/18	30/11/15	15/09/15	20/08/15	12/08/15	10/08/15	01/02/15
110	104	104	104	102	88	86	87	105	80

Accumulative Results

Vitamin D total (25-OH-Vitamin D3)

03/03/21	20/09/18	30/11/15	10/08/15	01/02/15	21/05/14	20/09/08
132.1	70.0	80.63	51	65	45.19	63.4 (NR greater or = 75 nmol/l)

Accumulative Results

Parathyroid Hormone (PTH)

20/08/15	10/08/15	01/02/15	20/09/08
4.040	6.916	4.8	3.71

Accumulative Results

Calcium

03/03/21	20/09/18	30/11/15	15/09/15	20/08/15	12/08/15	10/08/15	01/02/15	21/05/14	20/09/08
2.55	2.61	2.69	2.72	2.65	2.79	2.54	2.75	2.69	2.53

Figure 1. **Laboratory results from a patient's biochemical profile.**

Findings:

The calculated BMD of the AP spine L1 through L4 is 1.075 gm/sq. cm.
- T-score of - 1.2
- Z-score of - 0.8.

The calculated BMD of the left femoral neck is 0.899 gm/sq. cm.
- T-score of - 1.3.
- Z-score of - 0.4.

The calculated BMD of the right femoral neck is 0.864 gm/sq. cm.
- T-score of - 1.6.
- Z-score of - 0.6.

The calculated BMD of the left forearm is 0.738gm/sq.cm.
T-score of - 0.8.
Z-score of - 0.4.
The calculated BMD of the right forearm is 0.754 gm/sq.cm.
T-score of - 0.6.
Z-score of - 0.2.

Impression:
·According to WHO guidelines, this patient is considered osteopenic with moderate risk of fracture.

Figure 2. **DEXA scan results**

Bone mineral density of the lumbar spine is 1.103 g/cm2
T-score -0.1
Z-score 0.4

Bone mineral density at the left femoral neck is 0.891 g/cm2
T-score -1.1
Z-score 0.2

Bone mineral density at the right femoral neck is 0.846 g/cm2
T-score -1.4
Z-score -0.1

</CONCLUSION/>

The patients bone mineral density is within osteopenia. The estimated risk for major osteoporotic fracture 3.4% and for hip fracture 1.1%.

Figure 3. **BMD measurement**

DISCUSSION:

Currently, there are several published recommendations for the diagnosis and management of primary hyperparathyroidism. These recommendations emphasize establishing the presence of elevated serum calcium adjusted for albumin, elevated or non-suppressed PTH level, normal vitamin D levels, the absence of hypocalciuria, and assessment for potential organ involvement such as nephrolithiasis, nephrocalcinosis, renal impairment, and osteoporosis.

Most recommendations agree that symptomatic primary hyperparathyroidism should be treated surgically with parathyroidectomy and intraoperative examination of the other parathyroid glands (Khan, 2016), with the suggestion that parathyroidectomy has beneficial effects on the preservation of bone density, reduction in kidney stones, and stabilization of renal function (Khan, 2016). In less overt cases, surgical management should be offered to patients who have one or more of the following criteria regardless of symptoms: serum calcium 1mg/dl or 0.25 mmol/L above the upper limit of normal, evidence of skeletal involvement by DEXA scan diagnostic of osteoporosis or radiographic images showing reduced bone density, kidney involvement in the form of reduced creatinine clearance or eGFR < 60ml/min or nephrolithiasis evident on any imaging modality, increased urinary calcium excretion, or age less than 50 years (Bilezikian, 2022).

Based on the above recommendations, the patient presented in this case report should have been treated with parathyroidectomy at several points during the past 40 years, had these current recommendations been implemented at that time. Since the widespread implementation of current diagnostic and therapeutic recommendations worldwide, long-standing untreated primary hyperparathyroidism is uncommonly encountered in the clinical setting. A 2008 study followed 116 patients with mild primary hyperparathyroidism for 15 years, 59 of which were treated with parathyroidectomy and 57 of which remained untreated. After 15 years of observation, the authors concluded that while biochemical and BMD parameters remained stable for the first eight to ten years of follow-up of both patient groups, the effects of prolonged untreated hyperparathyroidism in the second group eventually started catching up with them in the form of loss of cortical bone mainly in the distal radius and femoral neck (Rubin, 2008). Remarkably, our patient continued to maintain his bone mineral density

over the almost 10-year interval between his two DEXA scans, despite having had at least one recorded kidney stone during that time. His calcium level continues to fluctuate, as does his PTH level, with the last measured PTH level being the highest reading available to me. Additionally, despite the frequent kidney stones and prolonged history of what is most likely primary hyperparathyroidism, he continues to have minimal renal involvement. Given this overall lack of significant organ involvement, and considering his long history with his condition, he remains reluctant to undergo a parathyroidectomy unless deemed necessary. This brings us to the question of whether we should reconsider the need for surgical intervention in some of our patients with primary hyperparathyroidism, especially those who have already had a long course with minimal impact on their end organs. In the age of precision medicine, we are moving away from treating our patients with a one-size-fits-all approach. We perhaps should be spending more time obtaining a more global picture of the patient's condition as well as their goals of treatment and preferences. Despite being an unconventional approach, in hindsight, it appears that the management route taken did not affect this particular patient detrimentally, raising the possibility that conservative management with close observation could be an option for select patients despite meeting surgical criteria.

This case prompts a critical reflection on the evolving landscape of primary hyperparathyroidism management. While current guidelines advocate for surgical intervention based on established criteria, the presented patient challenges this paradigm, demonstrating a lengthy disease course with minimal end-organ involvement. In the era of precision medicine, adopting a more individualized approach, considering the overall impact on the patient's quality of life, and respecting patient preferences become paramount. Continued close monitoring and shared decision-making with the patient align with contemporary trends in tailoring treatments to each patient's unique circumstances.

CONCLUSION

This case encourages further exploration of nuanced management strategies for primary hyperparathyroidism, recognizing that not all patients may fit the traditional treatment paradigm.

CONFLICT OF INTEREST

The author declared that there is no conflict of interest that is related to this study and this article.

DISCLOSURE

The author did not receive any form of commercial support, including compensation or financial assistance, for this case report. Additionally, the author has no financial interest in any of the products, devices, or drugs mentioned in this article.

ETHICAL APPROVAL

This study was approved by the Ethics Committee of the KAUH in Jeddah, Kingdom of Saudi Arabia with number Ref-60-24.

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