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Case Report

Beyond secondary hyperparathyroidism: Diagnosing primary parathyroid abnormalities in a patient with chronic kidney disease ☆

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ABSTRACT

Chronic kidney disease (CKD) is a complex medical condition that extends beyond the progressive decline in renal function. It is associated with mineral and bone disorders, notably secondary hyperparathyroidism due to dysregulated calcium and phosphate metabolism. However, distinguishing between secondary and primary hyperparathyroidism can be challenging. We report the case of a 74-year-old male with CKD, who presented with elevated serum levels of parathyroid hormone (PTH), CKD, and unexplained hypercalcemia, despite management for secondary hyperparathyroidism. Advanced imaging techniques revealed a primary parathyroid adenoma, subsequently confirmed by histopathology. The successful surgical resection of the adenoma resulted in the calcium and PTH levels falling into a normal range, highlighting the need for a careful differential diagnosis in CKD patients.

Introduction

Chronic kidney disease (CKD) is a global health concern with a multifaceted impact on patient health, including an increased risk of cardiovascular diseases, anemia, mineral and bone disorders (CKD-MBD), and other complications [1]. Among the spectrum of CKD-MBD, secondary hyperparathyroidism is a common condition, arising from dysregulated calcium and phosphate metabolism [2]. However, the occurrence of primary hyperparathyroidism due to parathyroid adenomas in CKD patients poses a diagnostic and therapeutic challenge, often complicating the management of mineral balance and bone health [3].

This case report presents a male patient with CKD, initially managed for secondary hyperparathyroidism, who was

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Table 1 – Laboratory findings.

Parameter	Value	Normal range	Notes
Calcium	11.5 mg/dL	8.5-10.2 mg/dL	Elevated; unresponsive to current regimen
Phosphorous	3.6		Normal
Urea	56 mg/dL	7-20 mg/dL	Elevated; CKD
Creatinine	1.9 mg/dL	0.6-1.2 mg/dL	Elevated; CKD
Potassium	4.5 mEq/L	3.5-5.0 mEq/L	Normal
HbA1c	7.37%	<5.7%	Moderate control; significant for diabetic nephropathy
PTH	290 pg/mL	15-65 pg/mL	Suggestive of hyperparathyroidism
Vitamin D	35.8 ng/mL	30-100 ng/mL	Normal; despite high PTH levels
ALP			Normal
GFR	45 mL/min	>90 mL/min	Moderate CKD

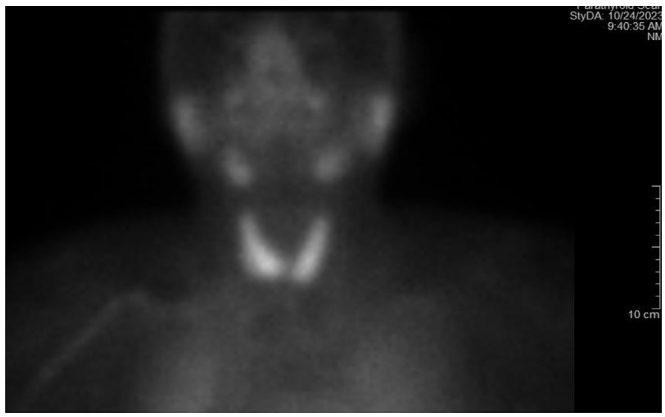

Fig. 1 – Normal trace uptake by the thyroid gland is evident.

later diagnosed with a primary parathyroid adenoma. The case underscores the critical need for a differential diagnosis in CKD patients presenting with unexplained hypercalcemia and highlights the role of advanced imaging techniques in diagnosing parathyroid adenomas. The successful surgical intervention led to significant improvements in the patient's biochemical parameters, emphasizing the importance of considering primary hyperparathyroidism in the differential diagnosis of CKD patients with mineral bone disorders. Through this case, we aim to contribute to the growing literature on the complexity of managing CKD-MBD and the potential for primary parathyroid adenomas to mimic or coexist with secondary hyperparathyroidism, thereby influencing treatment strategies and outcomes.

Case presentation

A 74-year-old male patient, with a past medical history significant for type II diabetes mellitus for 10 years and diabetic kidney disease diagnosed a year prior, presents with symptoms of dysuria and nocturia, seeking a second opinion for his CKD. He is currently taking febuxostat to manage elevated uric acid levels, carvedilol, omeprazole, and cinacalcet to treat his secondary hyperparathyroidism. A comprehensive metabolic panel including his renal function, uric acid levels, electrolytes, ALP, PTH, vitamin D, and eGFR was ordered. Normal phosphorus, vitamin D, elevated calcium, and PTH levels were noted (Table 1). The patient was not taking any calcium supplements.

Hypercalcemia in the absence of iatrogenic supplementation, associated with elevated PTH levels led to further diagnostic evaluations. A thyroid ultrasound revealed the presence of a small nodule in the posterior and inferior aspect of the right lobe, measuring up to 3 mm, with no vascular anomalies in Doppler examination.

The patient underwent an anterior and posterior planar Technetium-99m-sestamibi (MIBI) scintigraphy that showed normal trace uptake by the thyroid glands (Fig. 1). The 2-hours delayed phase scan revealed persistent uptake in the inferior right lobe correlating with a parathyroid adenoma (Figs. 2 and 3), consistent with the ultrasound findings.

The patient underwent a single gland parathyroidectomy and the pathology report confirmed the diagnosis of parathyroid adenoma.

Following the surgical excision of the adenoma, a significant reduction in PTH levels from 290 pg/mL to 41 pg/mL postoperatively was observed, confirming the diagnosis of primary hyperparathyroidism and the success of the intervention.

This was further confirmed upon histopathological examination of the excised gland. The adenoma predominantly

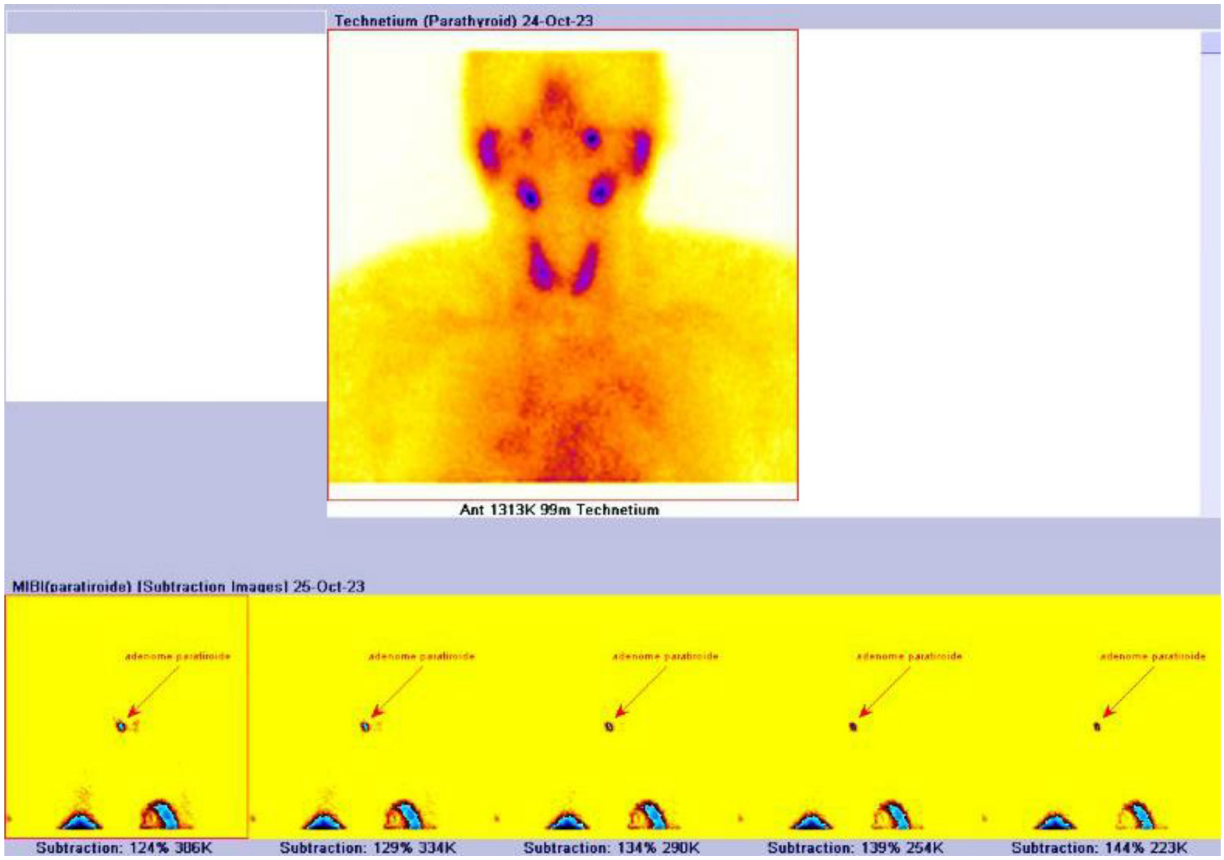

Fig. 2 – Persistent trace uptake in the inferior aspect of the right lobe, highly suggestive of a primary parathyroid adenoma.

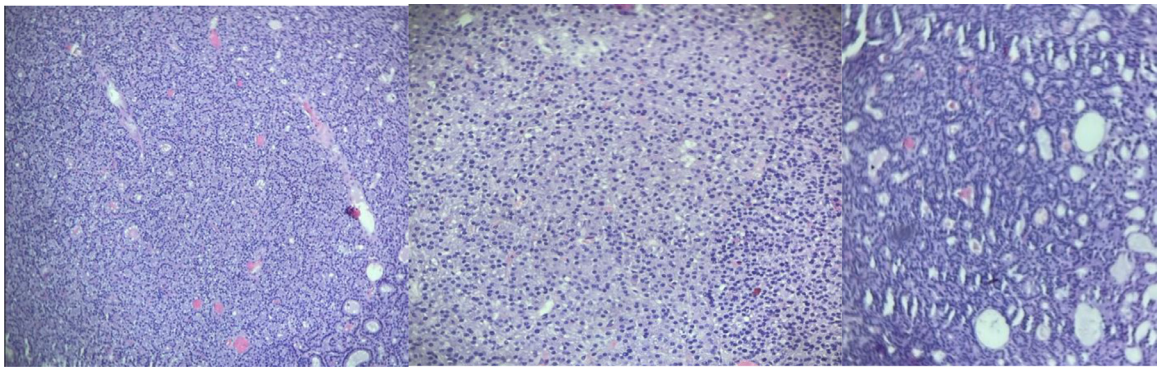

Fig. 3 – Histopathology of parathyroid adenoma.

consists of uniform chief cells arranged in solid sheets with eosinophilic, granular cytoplasm. Scant stroma is present, with occasional cystic degeneration. The benign nature is confirmed by the absence of capsular or vascular invasion, mitotic figures, or necrosis. (H&E stain, various magnifications).

Discussion

Chronic kidney disease (CKD) is a complex condition associated with a host of long-term complications including a higher prevalence of cardiovascular diseases, anemia, and disruption of calcium and phosphate metabolism [4–6]. CKD-mineral bone disease is characterized by anomalies in the calcium, phosphate, PTH, and vitamin D metabolism and represents an important challenge in the long-term management of CKD both in dialysis and nondialysis patients. CKD-MBD is associated with anomalies in bone turnover and mineralization, reduced bone growth and strength, pathological fractures, and as well as vascular calcification [7,8].

Serum PTH levels are the primary surrogate of CKD-MBD. Secondary hyperparathyroidism begins early in the course of chronic kidney disease and its severity increases as kidney

function declines [9]. PTH levels rise in response to decreased 1,25-dihydroxy vitamin D synthesis, increased FGF23 levels and decreased expression of vitamin D, reduced serum calcium and elevated phosphate levels, calcium-sensing, FGF23, and Klotho receptors in the parathyroid glands [10]. Elevated PTH levels have been found in approximately 60% of patients with GFR levels less than 60 mL/min. As GFR levels progressively decline below 60 ml/min, the elevation of PTH levels becomes more pronounced, but calcium and phosphate levels often remain normal in the early stages. The decrease in 1.25-dihydroxyvitamin D levels occurs more rapidly, largely due to increased FGF23 levels as opposed to reduced GFR [10,11].

Treatment of secondary hyperparathyroidism in nondialysis CKD patients is considered when PTH levels rise 2.3-3 times above the upper limit of normal [12]. Management strategies include modification of risk factors, dietary phosphate reduction, treatment of hyperphosphatemia and decreased vitamin D levels. Initiation of calcimimetics to mitigate elevated PTH levels is not recommended in nondialysis CKD patients, due to the high risk of hypocalcemia [13,14]. Our patient presented with an estimated GFR of 45 ml/min and elevated PTH levels 4-5 times above the normal range. Hypercalcemia despite the absence of calcium supplementation, normal vitamin D and phosphate levels were present as well. These findings suggested a primary parathyroid disorder, warranting further investigation. Normal alkaline phosphatase levels ruled out secondary bone pathology. Parathyroid scintigraphy revealed a parathyroid adenoma, leading to a diagnosis of primary hyperparathyroidism, which was confirmed by the pathology report following a single-gland parathyroidectomy. Calcium and PTH levels dropped back to normal in the postoperative period, further supporting the diagnosis of primary hyperparathyroidism.

A diagnosis of tertiary hyperparathyroidism was excluded in our patient, despite the presence of hypercalcemia and elevated PTH levels, as he was in the early stages of CKD and had a normal phosphate level. Tertiary hyperparathyroidism is characteristic of patients with end-stage kidney disease (ESKD) who do not respond to medical treatment and have high calcium, phosphate, and PTH levels [15].

The differential diagnosis between types of hyperparathyroidism in CKD patients can be very challenging as CKD itself is associated with elevated PTH levels [15,16]. However, it is crucial not to overlook the primary causes of PTH elevation. In cases lacking a clear clinical picture of CKD-MBD, a thorough evaluation is necessary to avoid a misdiagnosis, the progression of CKD due to persistent hypercalcemia, and unnecessary medications with potential side effects.

Conclusion

This case highlights the diagnostic challenges encountered in managing CKD-related hyperparathyroidism. It underscores the importance of taking into consideration primary hyperparathyroidism in CKD patients with atypical biochemical findings, particularly when clinical management fails to normalize calcium levels. Advanced imaging modalities help in establishing the diagnosis and guiding surgical intervention, averting potential complications of untreated primary hyperparathyroidism. We believe this case report will contribute to emphasizing the importance of adopting a vigilant approach in the management of CKD-related complications, particularly in terms of a tailored management of CKD-MBD.

Patient consent

We obtained written, informed consent for publication from the patient.

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