Chronic Kidney Disease in Parathyroid Adenoma and Post-Parathyroidectomy Hungry Bone Syndrome: A Case Report

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ABSTRACT

Hungry bone syndrome (HBS) is a clinical entity following parathyroidectomy among cases of primary parathyroid adenoma or secondary hyperparathyroidism. HBS is marked by persistent symptomatic hypocalcaemia in the postoperative period. The present report illustrates a case of a 35-year female with a history of recurrent nephrolithiasis. The patient was initially not screened for primary hyperparathyroidism and underwent multiple urological interventions including left nephrectomy. Postoperatively, an incidental finding of hypercalcaemia was correlated with parathyroid adenoma which was diagnosed by elevated parathyroid hormone (PTH) levels and radionuclide imaging. Following parathyroid resection, the patient developed clinically significant hypocalcaemia which was also marked by decreased PTH and persistently low levels of serum calcium, phosphate, and magnesium, raising suspicion of HBS. For this purpose, the patient was also hospitalised on two separate occasions. The patient was then extensively treated with vitamin D and calcium supplements which gradually stabilised her calcium levels. Bisphosphonate therapy was not implemented in this patient.

Key Words: *Chronic kidney disease, Hyperparathyroidism, Hungry bone syndrome, Parathyroidectomy, Hypocalcaemia.*

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INTRODUCTION

Hungry bone syndrome (HBS) comprises severe hypocalcaemia following parathyroidectomy (PTX) due to a rapid drop of parathyroid hormone (PTH) after previous prolonged elevated levels and associated bone remineralisation.[1] Osteoclastic resorption leads to a decrease in new remodeling sites and space leading to a consequent gain in bone mass. This is believed to be the cause of the rapid, profound, and sometimes prolonged decrease in serum minerals.[2] The incidence of HBS in primary hyperparathyroidism is 15-20%. Usually, HBS is more prevalent in patients with renal insufficiency.[3] However, there are no well-reported cases of HBS in Pakistan. This case report is according to CARE guidelines.[4]

CASE REPORT

A 35-year female presented to the urology outpatient department with the complaint of bilateral flank pain for 1.5 months, associated with a markedly reduced ability to mobilise without support.

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She was a previously diagnosed case of chronic kidney disease (CKD) Stage 3B secondary to bilateral nephrolithiasis. The patient also reported a positive family history of nephrolithiasis among two siblings. Her baseline creatinine was 2.3 mg/dL. Ultrasound kidney, ureters and bladder (KUB) showed bilaterally hydronephrotic kidneys with multiple right renal and left ureteric stones. Her DTPA scan reported a non-functioning left kidney and a hypofunctional right kidney. The patient's parathyroid profile was not evaluated at baseline and no underlying aetiology was documented for nephrolithiasis. The CT scan showed a brown tumour of the femur (Figure 1).

The patient initially underwent multiple urological procedures including cystoscopy and bilateral DJ stenting (8th March 2023), right percutaneous nephrolithotomy (PCNL) on 4th July 2023 followed by total left nephrectomy and DJ stent removal on 15th August 2023. Before nephrectomy, the patient was also reviewed by the nephrology team on 20th July 2023, during which she was advised for medical optimisation of deranged renal function tests. Moreover, follow-up was advised along with serum calcium and parathyroid profile. Following nephrectomy, the patient's serum profile showed persistently raised levels of calcium (12.8-14.0 mg/dL), magnesium (2.6-2.9 mg/dL), and phosphate (5.2-5.0 mg/dL). Incidentally, the baseline intact PTH (iPTH) level was 2,126 pg/ml and the alkaline phosphatase level was also elevated to 581 U/L. Following initial intravenous hydration, the patient was referred to the endocrinologist who initiated treatment with 30 mg of oral Cinacalcet once daily and vitamin D 5,000 IU per week.

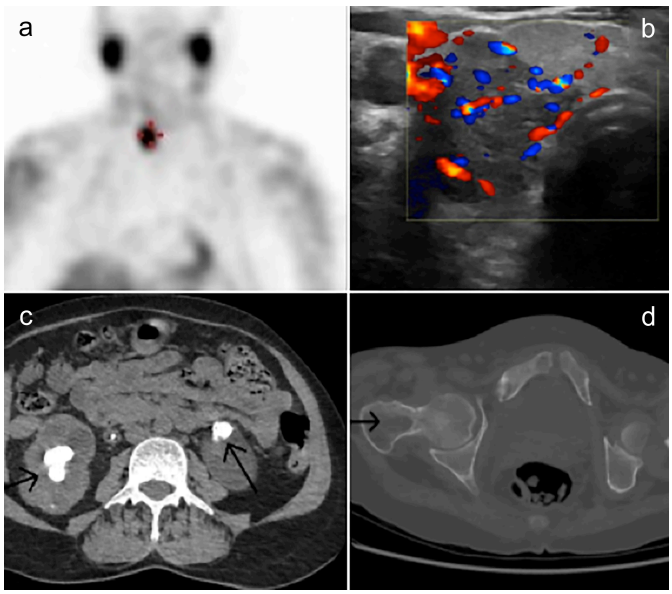

Figure 1: (a) SPECT scan of parathyroid adenoma (b) Hypervascular parathyroid adenoma on ultrasonography doppler flow (c) CT scan showing bilateral nephrolithiasis (d) CT scan showing brown tumour of bone.

Following the endocrinology review, the patient underwent a SPECT imaging scan on 30th August 2023 which revealed a markedly hyperfunctioning right inferior parathyroid gland. Right inferior parathyroidectomy was subsequently undertaken on 13th September 2023. In the aftermath of parathyroidectomy, the patient was hospitalised on 24th September 2023 with worsening numbness in peripheral extremities. No positive classical signs of hypocalcaemia (carpopedal spasm, Chvostek sign, and Trousseau sign) were observed. Post parathyroidectomy, the patient developed significantly reduced levels of calcium (6.1 mg/dL), magnesium (1.4 mg/dL), and phosphate (2.1 mg/dL) which fulfilled the criteria for HBS. Concomitantly, iPTH was lowered to 370 pg/ml. Calcium and magnesium were substituted intravenously in the emergency department. Subsequently, the patient was advised dietary substitution of calcium, magnesium, and phosphate as well as oral calcium and vitamin D supplements. During the most recent follow-up (10th November 2023), all laboratory values were normalised as serum calcium at 9.2 mg/dL, magnesium 2.5 mg/dL, and phosphate 3.6 mg/dL. Moreover, serum creatinine was also stabilised at 2.6 mg/dL.

DISCUSSION

HBS is characterised by a drop in serum calcium levels to below 8.4 mg/dL which potentially persists for longer than 4 days following parathyroid resection.[3] During the phase of primary hyperparathyroidism, serum calcium and phosphate levels are disproportionately raised secondary to an increased rate of bone resorption. Once the glands are resected, the circulating levels of PTH fall and calcium and phosphate minerals are vigorously redirected into the osseous compartment. HBS typically leads to symptomatic hypocalcemia which was also evident in the present case.[5]

The onset of HBS was marked by a substantially lower serum level of vitamin D during the pre-parathyroidectomy phase. Furthermore, this is associated with markedly higher levels of serum phosphate, magnesium, and alkaline phosphatase prior to parathyroidectomy.[6] These findings were also notable in the present case. Evidence from other studies contradicts this statement, thereby showing that serum vitamin D levels do not act as an independent predictor of HBS in primary hyperparathyroidism.[7] Nonetheless, preoperative supplementation of vitamin D has been correlated with a relatively lower risk of HBS which is primarily due to a significant perioperative reduction in the plasma levels of PTH.[8] Interestingly, our patient's preoperative iPTH levels dropped from 2,126 pg/ml to 1,791 pg/ml after the initiation of vitamin D and Cinacalcet therapy.

In addition to vitamin D supplementation, the role of bisphosphonates in ameliorating the overall risk of HBS has often been debated by endocrinologists. In this perspective, multiple case reports and prospective case-control studies have been documented.[6] Studies have indicated that preoperative use of intravenous bisphosphonates for either shorter or prolonged periods leads to a significantly lower probability of developing HBS.[9] In one comparative analysis, patients receiving bisphosphonate treatment failed to experience HBS in contrast to approximately half of the patients, who developed HBS without receiving bisphosphonates. Furthermore, preoperative bisphosphate therapy has also been shown to lower the overall extent of post-parathyroidectomy calcium supplementation.[10]

In this case study, the patient's vitamin D levels were not measured at baseline which failed to establish any correlation between preoperative vitamin D deficiency and subsequent HBS. Furthermore, although the use of bisphosphonate therapy was considered at one point by the nephrology team, no such treatment was initiated. Another major concern in this case was a missed initial diagnosis of primary hyperparathyroidism. Had the patient's PTH profile been tested before commencing urological intervention, parathyroidectomy could have been undertaken much earlier which could have improved the overall prognosis of her CKD. This, in turn, emphasises the role of routine chemical analysis of renal stones following their surgical removal.

In conclusion, this case report describes an interesting case of HBS while also highlighting a few important perioperative determinants of the condition. These indicators of HBS potentially warrant a detailed investigation through large clinical trials.

PATIENT'S CONSENT:

Informed consent was obtained from the patient to publish this case.

COMPETING INTEREST:

The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:

MS, RGG: Manuscript writing.
HN: Editing and proofreading.
ARN: Supervision.

HA: Conceptualisation.
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