CASE REPORT

Acute kidney injury associated with hypercalcaemic crisis in a patient with primary hyperparathyroidism

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SUMMARY

Parathyroid or hypercalcaemic crisis is a rare presenting manifestation of primary hyperparathyroidism and usually seen in relation to parathyroid carcinoma and multiple myeloma. We present a middle-aged woman with extreme hypercalcaemia due to parathyroid adenoma presenting as acute kidney injury. This case highlights the need to consider primary hyperparathyroidism in differentials of a patient presenting with severe hypercalcaemia and renal dysfunction. Also this is the second reported case in literature of a patient surviving such extreme hypercalcaemia due to parathyroid adenoma.

BACKGROUND

Primary hyperparathyroidism (PHPT) is usually asymptomatic and routinely detected on biochemical evaluation. Parathyroid/hypercalcaemic crisis is a rare, severe life-threatening complication of PHPT defined as serum calcium greater than 15 mg/dL (≥ 3.75 mmol/L) with signs and symptoms of acute calcium intoxication.¹ Patients usually present with end organ damage mostly affecting central nervous system, cardiac, gastrointestinal and renal functions. We present a case of parathyroid crisis with serum calcium as high as 25 mg/dL (6 mmol/L) presenting with acute kidney injury due to PHPT. A benign curable parathyroid adenoma to present with hypercalcaemic crisis as seen in our case is rare, and it is usually described in relation with parathyroid carcinoma and multiple myeloma. The highlight of the case is that the patient survived such extreme hypercalcaemia and had complete recovery of renal functions after parathyroidectomy.

CASE PRESENTATION

A 47-year-old woman with no previous comorbidities presented with generalised body aches, lethargy and worsening epigastric discomfort for 6 months. She had also developed increased thirst, urinary frequency, reduced appetite, severe nausea, vomiting and constipation over 6 months. The patient had consumed multiple over-the-counter analgesic preparations for bony pains without much relief. Laboratory evaluation revealed haemoglobin 10.2 (12–18 g/dL), severe hypercalcaemia with serum calcium of 25 (8.5–10.2 mg/dL) and corrected calcium of 25.4 mg/dL (6 mmol/L), serum phosphorus of 4.7 (2.7–4.5 mg/dL) and serum creatinine of 2.9 (0.5–1.2 mg/dL). Vitamin D (25 OH D3) was 38 (11–43 ng/mL), intact parathyroid hormone

(iPTH) was 1584 (16–87 pg/mL). A 24-hour urine calcium was 430 mg/day (50–300 mg/day). Neck ultrasound demonstrated encapsulated hypoechoic mass in relation to mid and lower pole of right lobe of thyroid gland and lower pole of left lobe of thyroid gland suggestive of multiglandular parathyroid involvement. Radionuclide parathyroid scintigraphy confirmed parathyroid adenoma in relation to lower pole of left lobe and upper pole of right lobe of thyroid (figure 1). Her symptoms, together with very high serum calcium (corrected serum calcium of 25.4 mg/dL) and high PTH, suggested that she was in parathyroid crisis. After admission she was started on intravenous fluids to maintain urine output of 100–150 mL/hour and single dose of intravenous pamidronate 60 mg was administered over 4 hours on day 2 of admission. Her ECG showed shortened QT interval of 0.36 s (normal corrected QT 0.37–0.44), hence calcium-free haemodialysis was given via femoral catheter of 4 hours' duration with a blood flow rate of 250 mL/min and dialysate flow rate of 500 mL/min. In view of ongoing hypercalcaemia, the patient required one more session of calcium-free haemodialysis of 4 hours' duration on the fourth day of admission. After haemodialysis, corrected serum calcium decreased to 13.5–14 mg/dL and serum creatinine decreased to 1.6–1.8 mg/dL and further haemodialysis was withheld. Renal biopsy was done on day 6 of admission as serum calcium was stuck at 1.6–1.7 mg/dL and did not decrease further as per natural expected course of acute kidney injury and it revealed nephrocalcinosis and chronic interstitial nephritis. Guided by preoperative ultrasonography and sestamibi scan, bilateral neck exploration was performed and right entire parathyroid gland and left inferior parathyroid gland were removed on day 10 of admission. Left superior gland was left intact. Histopathological examination from the right superior and inferior gland showed no features of adenoma (both weighed 200 mg) and were histologically normal. However, left inferior gland showed features of benign adenoma (weighed 1600 mg).

DIFFERENTIAL DIAGNOSIS

Differentials of acute kidney injury with hypercalcaemia considered in this case were multiple myeloma, parathyroid carcinoma, humoral hypercalcaemia of malignancy and parathyroid adenoma.

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Figure 1 Technetium-99 m sestamibi scan revealed hypermetabolic lesions suggestive of parathyroid adenoma in relation to lower pole of left lobe and upper pole of right lobe of thyroid.

OUTCOME AND FOLLOW-UP

The patient's appetite, polyuria and general well-being improved. Her body aches and constipation subsided. Serum calcium and iPTH levels on months 1 and 12 after surgery were 7.2 and 8.6 mg/dL and 96 and 70 pg/mL, respectively. Serum creatinine is maintained between 0.8 and 1 mg/dL during 1-year follow-up. The patient had persistent hypocalcaemia for 2 months after surgery which became eucalcaemic later with calcium supplements.

In cases of benign parathyroid disease, it is often unclear what leads to the exacerbation of the condition. In some cases, intrinsic parathyroid factors, such as rapid growth with partial necrosis or infarction of the parathyroid adenoma, may be the reason. Acute cystic degeneration of a pre-existing parathyroid adenoma can result in marked acute elevations of serum PTH levels with subsequent hypercalcaemic crisis [15]. This can be explained by the sudden release of large amounts of hormone from damaged epithelium and may have been the

DISCUSSION

Hypercalcaemic crisis is a rare life-threatening complication of PHPT occurring in 1%–2% of patients.² PHPT usually presents with mild hypercalcaemia and diagnosed incidentally on routine investigations. The biochemical profile of our patient mimicked parathyroid carcinoma as parathyroid crisis is seen more commonly in parathyroid carcinoma. Parathyroid adenoma presenting with preoperative PTH 1584 ng/mL and life-threatening hypercalcaemia as in our case is rarely reported in literature. Prior to our case, Marienhagen *et al* had reported a patient surviving extreme hypercalcaemia due to parathyroid adenoma with a serum calcium of 27 mg/dL.³

Management of patients in parathyroid crisis consists of emergency measures to acutely decrease serum calcium. First-line therapy consists of volume expansion with isotonic saline at an initial rate of 200–300 mL/hour which is later adjusted to maintain a urine output of 100–150 mL/hour.⁴ Calcitonin at dose of 6–8 IU/kg every 6 hours acts rapidly and lowers serum calcium by 1–2 mg/dL. However, it is not readily available in our region and has side effect of tachyphylaxis by receptor down-regulation. Hence, its efficacy is limited to first 48 hours only.⁵ Bisphosphonates take 2–4 days for maximum effect, so they are usually given along with saline hydration and calcitonin which

act more rapidly. And the effect of bisphosphonates lasts for several weeks which can lead to postoperative hypocalcaemia.⁶ Pamidronate is used most commonly in dose of 30–90 mg intravenous infusion administered over 4–6 hours.⁷ When serum calcium fails to decrease with the standard treatments or if there is cardiac/neurological impairment, haemodialysis is effective as a last resort to rapidly lower serum calcium.^{8,9} The use of low calcium dialysate of 1.25 mmol/L is found to be more effective than standard calcium dialysate of 1.5 mmol/L.¹⁰ Some institutions including ours perform calcium-free haemodialysis in acute hypercalcaemic crisis.^{8,9} However, some argue against use of calcium-free haemodialysis as haemodynamic instability and hypotension may occur due to suppression of myocardial contractility.¹¹

Medical therapy should be followed by urgent parathyroidectomy which remains the cornerstone of management in hypercalcaemic crisis due to PHPT.¹²

Patient's perspective

After the surgery, I recovered from almost bed bound state and taking multiple over the counter drugs to being normal. Didn't know the small gland in the neck was doing all this havoc.

Learning points

- ▶ Parathyroid adenoma presenting as hypercalcaemic crisis is rare. Always suspect and rule out parathyroid carcinoma.
- ▶ Surgery is the cornerstone of management and should not be delayed.

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