Primary Hyperparathyroidism with Markedly Elevated Serum Calcium and PTH - Clinical and Surgical Implications For Possible Parathyroid Carcinoma

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ABSTRACT

Primary hyperparathyroidism (PHPT) can be caused by a single adenoma, multiple adenomas, hyperplasia, or occasionally by parathyroid carcinoma.

Primary hyperparathyroidism associated with grossly elevated serum calcium levels (PTH) and exceptionally high serum calcium levels, raises the suspicion for parathyroid carcinoma.

We present our series of four patients with PHPT with extremely elevated serum calcium and PTH levels. Clinical workup and perioperative management is discussed and operative strategy is suggested.

The treatment of extreme hyperparathyroidism and hyperparathyroidism, including the role of en bloc resection with ipsilateral thyroid lobectomy, as well as the importance of intraoperative PTH assay in confirming complete removal are emphasized.

INTRODUCTION

Primary hyperparathyroidism (PHPT) is the most common cause of elevated parathyroid hormone (PTH) with the majority of cases attributed to a single parathyroid adenoma.

They often present with elevated levels of serum calcium greater than 14mg/dL. Corresponding parathyroid hormone levels can be abnormally elevated with ranges from 300 to 1000 pg/ml.

Increased PTH and hypercalcemia can lead to both short term and long term adverse affects.

In the acute setting, hypercalcemia causes tiredness, confusion, unstable gait, constipation, decreased appetite, increased urination, and bone pain.

Long term effects of hyperparathyroidism can lead to arterial hypertension, renal failure, and osteoporosis from continued bone resorption resulting in pathologic fractures (6), convulsions, and even cardiac states.

Peri-operative management of these patients is extremely important and should be undertaken with the medical or endocrinology team. Patients often are admitted pre-operatively to lower their serum calcium to prevent intraoperative complications.

Hypercalcemia is also a risk postoperatively, and although uncommon, hungry bone syndrome can develop due to hypocalcemia, hypophosphatemia and hypomagnesemia on laboratory testing and clinically with parasthesia, lip and finger tingling, tetany and seizures (7).

Parathyroid carcinoma should be considered when pre-operative calcium is 14mg/100ml or 2.4mg/dl above the upper limit in association with elevated PTH levels. This possible scenario requires the surgeon to make critical decisions as to the extent of surgery to be recommended.

METHODS AND MATERIALS

We present two of the four cases of hyperparathyroidism with very elevated calcium and PTH levels. Although all cases were postoperatively confirmed as benign adenomas, suspicion for parathyroid carcinoma exists. A management strategy algorithm is proposed.

Case 1 - A 16 year old female presented to our clinic with symptomatic hypercalcemia including nausea, vomiting, and renal stones referred from the endocrinology service. She had undergone lithotripsy and renal stent placements. Her serum calcium over the previous year ranged from 10-17.2 mg/dL. A Tc-sestamibi scan was performed which noted a solitary large focus of increased activity adjacent to the left trachea in the thyroid bed (Figure 3). A thyroid ultrasound also noted a mass in the lower two-thirds of the left lobe (Figure 4).

She was admitted preoperatively to endocrinology for appropriate management of her hypercalcemia. We counseled the patient on our surgical approach involving a parathyroidectomy, parathyroidectomy, and possibly a thyroid lobectomy and/ or paratracheal node dissection.

Case 2 - An 18 year old male was referred from an urgent care facility for flank pain and hematuria. A CT scan of the abdomen that demonstrated renal stones. His serum calcium was 15.5 mg/dL and his PTH 655 pg/mL. He was admitted to hospital for IV Hydration and calciitonin. His calcium levels dropped over 6 days to 9.4 mg/dL. His sestamibi scan and an MRI prior to evaluation demonstrated a 2x3 cm mass just inferior to the right thyroid lobe (Figure 1, 2). A discussion with the patient regarding the possibility of parathyroid carcinoma in view of the high serum calcium and parathyroid levels was performed pre-meditatively. A 3-cm right sided parathyroid gland was indentified sitting just medial and deep to the carotid on the lateral surface of the esophagus. No infiltrative features were noted. Intra operative PTH dropped from 663 pg/mL pre-incision to 55 pg/mL, 20 minutes post excision. A 5-gram adenoma was confirmed.

DISCUSSION

The standard of care for primary hyperparathyroidism is surgical removal of all hyperfunctional parathyroid tissue particularly for patients with symptomatic primary hyperparathyroidism. Surgical indications have also been outlined for asymptomatic patients with hyperparathyroidism and include: serum calcium concentration 1.0mg/dL above the upper limit of normal, reduction in creatinine clearance of 30% (or more recently defined as GFR<60mL/min), bone mineral density – t score < -2.5 at any site, and age <50 years old (5.6). Although 24-hour urine calcium excretion of >400mg was an original indication, the more recent 2008 guidelines suggest assessing urine calcium simply to rule out familial hypo-calcic hypercalcemia, and not as an indication for surgical intervention(5,6). This series of patients with very elevated calcium levels emphasizes the importance of preoperative control of hypercalcemia. Initial treatment of severely hypercalcemic patients (3-4mg/dl above the upper limit of normal) requires medical management with rehydration, usually with intravenous saline, early mobilization, and diuresis with close monitoring of cardiovascular status and serum electrolytes(5,6). Intraoperatively, the anesthesiologist must be mindful of the effects hypercalcemia. Avoidance of acidosis must be kept in mind, as hypercalcemia can result in resistance to competitive blockade by certain paralytics(5). We tend to perform parathyroidectomies without paralytics as we utilize the intraoperative nerve monitor.

CONCLUSIONS

Markedly elevated hypercalcemia and PHPT requires preoperative, intraoperative, and postoperative planning and should lead to a greater suspicion for parathyroid malignancy.

Due to the histological challenge in diagnosis, we recommend low threshold for intraoperative decision making, with consideration of en bloc resection of the adjacent thyroid lobe and parathyroid lesion. We also recommend not overlapping the importance of preoperative informed consent with patient education and counseling.

REFERENCES

1. [References provided in the text]