CLINICAL VIGNETTE

Hypercalcemic Crisis in Primary Hyperparathyroidism

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Introduction

Hypercalcemia manifests with non-specific symptoms including urinary stones, constipation, malaise, generalized fatigue, bone pain, cardiac arrhythmias and mental status changes. Hyperparathyroidism (HPT) is a common cause of hypercalcemia. Etiology of HPT can be broken down to parathyroid adenoma (80%), primary parathyroid hyperplasia (15%), and the remaining 5% due to a mixture of parathyroid carcinoma and inheritable neoplastic disorders.[1] Hypercalcemic crisis is defined as symptomatic hypercalcemia greater than 13-14 mg/dL.

Clinical Vignette

A previously healthy 45-year-old male presented to a community hospital with one week of progressive generalized weakness and malaise. Review of systems was remarkable for myalgias, decreased oral intake, constipation, and increased urinary frequency. He was afebrile with blood pressure 93/61, heart rate 122 beats per minute, respiratory rate 19 breaths per minute and oxygen saturation of 97% on room air. He appeared lethargic but was responding appropriately and was oriented. No other abnormalities were noted on exam.

Initial labs revealed severe hypercalcemia of 21.8 mg/dL. Additional evaluation revealed multi-organ failure, manifested by oliguric acute renal failure (creatinine 5.1 mg/dL), severe sepsis (lactate 2.6 mmol/L, leukocytosis of 36.1/uL with 10.7% bands), and myocardial injury (troponin 19.07 ng/mL). Other lab results included serum hemoglobin 14.1 g/dL, platelet count 529,000/uL, sodium 127 mmol/L, potassium 3.3 mmol/L, blood urea nitrogen 87 mg/dL, magnesium 1.7 mg/dL, phosphorus 5.0 mg/dL, and albumin 1.5 g/dL. Four liters normal saline boluses were given in the initial 4 hours followed by continuous intravenous fluids. Electrocardiogram showed sinus tachycardia, diffuse ST depressions, and prolonged QT interval. Standard initial therapy for NSTEMI was started. Bedside echocardiogram showed preserved ejection fraction and no wall motion abnormalities. Repeat vital signs following fluid boluses showed resolution of hypotension and tachycardia.

Six hours after presentation, the patient acutely decompensated into pulseless electrical activity. The patient expired from cardiac arrest after 90 minutes of advanced cardiac life support and cardiopulmonary resuscitation. Repeat serum calcium drawn during resuscitation was 13.3 mg/dL. Serology later revealed elevated serum PTH of 3960 pg/mL (ref 15-65 pg/mL), with no monoclonal proteins identified on immunofixation. These findings were consistent with primary hyperparathyroidism.

Discussion

Hypercalcemic crisis poses the greatest risk for organ damage to the kidneys and brain presenting with acute renal failure and somnolence/coma. Initial management of symptomatic moderate – severe hypercalcemia necessitates intravenous fluid resuscitation, calcitonin, and bisphosphonates.[2,3] Saline infusion should begin at 200-300 nL/hour and subsequently be adjusted to maintain a urine output of 100-150 mL/hour. Because severe hypercalcemia typically causes extreme hypovolemia, loop diuretics have fallen out of favor. Calcitonin is effective within 2 hours but carries the risk of tachyphylaxis with prolonged use for 48-72 hours and possible rebound hypercalcemia after 24 hours.[4] Conversely, the maximal effect of bisphosphonates would be apparent about 24 hours after initiation. Denosumab can be considered in hypercalcemia of malignancy refractory to bisphosphates. Glucocorticoids can be used to manage of hypercalcemia secondary to lymphoma, granulomatous disease, and vitamin D intoxication and is effective within 2-3 days. Emergent hemodialysis with low-calcium or calcium free dialysate is recommended in severe life-threatening hypercalcemia or in oliguric and anuric patients unable to achieve adequate calciuresis.[4,5] Some literature advises low-calcium dialysate to avoid more sudden calcium shifts. However, the significance of this calcium shift is unclear. In the study by *Sonoda and colleagues*,[6] 89 patients with calcium greater than 12 and no history of structural heart disease were found to have no cardiac arrhythmias during hospitalization despite universal ST segment elevations, which can masquerade as acute myocardial infarction.[7]

Resection of the parathyroid-producing lesion is curative of HPT-related hypercalcemia with a quantifiable decrease in PTH levels post-operatively.[8,9] However, the optimal timing of surgery when urgent surgery is indicated, has been variably reported in the literature. The reported optimal timing for urgent surgery has ranged from 48 hours to 2 weeks, pending medical optimization with intravenous fluids, bisphosphonates, calcitonin and hemodialysis, as indicated.[2,3,10-12]

The high mortality of hypercalcemic crisis cannot be understated. In the 1967 systematic literature review of hypercalce-

mic crisis cases by Macleod and colleagues,[13] 52 of 86 cases had a fatal outcome, approximately a 60% mortality rate. More recent retrospective reviews of mortality of cases of post-parathyroidectomy patients presenting with hypercalcemic crisis due to parathyrotoxicosis note a mortality rate of at most 8%.[2,9,11] Even with appropriate management and serial laboratory findings consistent with decreasing serum calcium, patients can acutely decompensate due to significant multi-organ involvement.[14-16] Consequently, early management of hypercalcemic crisis relies on diagnosis, restoration of euvolemiaa, aggressive correction of serum calcium, close monitoring, and involvement of several specialty teams as these patients can be deceptively clinically unstable.

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