A 56-Year-Old Man with Vertigo and Hypercalcemia

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A 56-year-old Man with a past medical history significant for lower back pain and GERD was admitted to the hospital for dizziness and laboratory abnormalities.

Five days prior to admission, the patient noted that he felt dizzy and unsure while walking. These symptoms persisted without change and he went to see his primary care doctor the day prior to admission. The patient was given meclizine for his dizziness and routine labs were drawn. He received a call from his doctor on the day of admission instructing him to be evaluated for an elevated serum calcium.

He described his primary complaint as if his surrounding were moving. He did not complain of lightheadedness or syncope and reported that his symptoms did not change with position. The symptoms did not change if he closed his eyes or when he sneezed, coughed, or strained. There was no associated nausea or vomiting.

His medical history was significant for severe GERD for which he took ten to fifteen over-the-counter calcium carbonate tablets daily with moderate symptom relief however had not had a medical evaluation for these symptoms. He also reported severe lower back pain that he attributed to his strenuous occupation which began approximately nine months prior to admission. At first, his back pain was alleviated by occasional ibuprofen use, however at present, the patient was taking six to eight 200 mg over-the-counter tablets of ibuprofen daily. He had not been evaluated medically for his back pain. He also reported unilateral glaucoma as a child and had required enucleation of his right eye. Recently, he had arthroscopic exploration of his left knee and was aware that he would eventually require knee replacement.

He reported that he knew of no allergies to medications and was only taking the over-the-counter medications as above. His family history was notable only for multiple members of his family with coronary artery disease at a young age. He knew of no family members with cancer or kidney disease. He occasionally drank alcohol at social functions and had never been a tobacco user. He works in maintenance and lives with his wife and daughter.

His review of systems was generally unremarkable. He reported that he had decreasing urinary stream and volume and increasing frequency during the past month. He reported no weight loss or constitutional symptoms.

The temperature was 97.3ºF, the pulse was 73 and regular, the blood pressure was 159/70 andd he was breathing comfortable at 16 respirations per minute. His oxygen saturation was 94% on room air.

On physical examination, he was a pleasant and mildly obese man in no distress. He was normocephalic, his left pupil reacted briskly to light; he had a prosthetic in his right enucleated eye. There was no notable nystagmus. The heart, lung, abdominal, and extremity examinations were all unremarkable. His rectal examination revealed normal sphincter tone and an asymmetric nodule on the left lobe approximately 1 cm in diameter. His neurologic exam was non-focal and his cranial nerves were intact.

On admission, laboratory values of note were a serum calcium of 15.6 mg/dL and a creatinine of 3.2 mg.dL. The remainder of his chemistry and hematologic values were within normal limits. An initial troponin drawn in the emergency department was normal.

He was admitted with a diagnosis of hypercalcemia and for a thorough evaluation of an underlying oncologic or endocrine process. His initial treatment with 4 mg of zoledronic acid, 400 international units of salmon-calcitonin, as well as aggressive intravenous hydration. He was placed on 40 mg intravenous pantoprazole for relief of his reflux symptoms and he was provided with acetaminophen for his back pain. On hospital day 2, the serum calcium level was 8.3 mg/dL and his creatinine was 1.8 mg/dL.

A CT scan of his head was performed which was read to have no intracranial pathology. His initial lumbar x-ray was read as spondylothiasis, likely compression fractures at L4 and L5. A follow-up MRI of lumbar spine showed multilevel disc bulging, protrusions, and facet arthropathy with moderate bilateral foraminal narrowing, however there was no evidence of compression fracture as previously suggested.

A CT of the chest and abdomen were performed and showed no acute pathology. The radiologist noted that severe gastroesophageal reflux was evident by contrast refluxing into the esophagus as well as faint nonobstructing calculi in the lower pole of the right kidney. A renal ultrasound revealed no hydronephrosis or renal calcifications, and there was clear cortical medullary differentiation.

The results of his serum parathyroid hormone, vitamin D level, and prostate specific antigen were all within normal limits. Urine electrolytes were evaluated and the calculated fractional excretion of sodium was 7.2%, suggestive of acute tubular necrosis. Of note, his total cholesterol was 291 mg/dL and his low density lipoprotein was 200 mg/dL.

The consulting urologist felt that his exam findings may be consistent with asymmetric benign prostatic hypertrophy and planned a transrectal biopsy as an outpatient. The consulting gastroenterologist performed esophagogastroduodenoscopy and the results were consistent with Barrett's esophagus secondary to a hiatal hernia. The patient was continued on pantoprazole.

Without evidence of an oncologic process or elevated parathyroid hormone, the diagnosis of milk-alkali syndrome was made. High dose ibuprofen likely resulted in acute tubular necrosis and a decreased ability to excrete the high doses of calcium that the patient was ingesting. The hypercalemia and acute renal failure resolved and the patient was discharged on pantoprazole, atorvastatin, and acetaminophen as needed for pain. He was instructed to stop taking calcium carbonate and non-steroidal anti-

inflammatory medications. Appointments with gastrointestinal, urologic, and cardiovascular specialists as well as for a stress test were made for the patient.

Discussion

There is an extensive list for the differential diagnosis of hypercalcemia. Hyperparathyroidism is the most common cause in ambulatory patients and malignancy is the most common cause in hospitalized patients. The differential of hypercalcemia can be divided into three major categories. Increased bone resorption can be caused by hyperparathyroidism, cancer, hyperthyroidism, and Paget's disease. Increased calcium absorption can be caused by increased calcium uptake and hypervitaminosis D. Miscellaneous causes of hypercalcemia include drug toxicity and conditions such as pheochromocytoma.

The presentation of this patient with milk-alkali syndrome and underlying renal insufficiency has become rather rare since the introduction of modern ulcer therapy. It has, however, increased in frequency with more use of calcium carbonate for osteoporosis prophylaxis. Subsequently, this syndrome has experienced an increased prevalence in females, whereas before it was more common in men . Prior to 1990, the milk-alkali syndrome accounted for less that 2% of admissions related to hypercalcemia with a small reported rise during the 1990s. Since calcium has various roles in the body including cardiac and smooth muscle contraction, and in platelet aggregation and function, proper treatment and management of hypercalcemia is imperative.

In this patient, milk-alkali syndrome was suspected as the cause of hypercalcemia after ruling out other causes of hypercalcemia. In one case series, five patients who had milk-alkali syndrome patients were ingesting large quantities of calcium and absorbable alkali and presented with the triad of hypercalcemia, metabolic acidosis, and renal failure. In two of these patients, renal failure resulted in the need for dialysis. Kapnser, et al. reported on 297 heart and heart-lung transplant recipients who were being treated with calcium carbonate after cardiac transplantation. This treatment resulted in sixty-five patients who developed serious hypercalcemia after transplantation. Thirty-one of these patients experienced alkalosis and thirty-seven of had renal impairment.

The use of calcium in patients with preexisting renal insufficiency is an important consideration. Four patients in a case report with mild, asymptomatic chronic renal failure took daily over-the-counter antacids and required hospital admission for hypercalcemia. It is also imperative to monitor calcium use in pregnant patients. Maternal prolonged hypercalcemia secondary to primary hyperparathyroidism can affect the fetal circulation and lead to suppression of fetal parathyroid function and lead to neonatal hypocalcemia and tetany or may result in spontaneous abortion and stillbirth. Therefore, monitoring calcium intake in pregnant patients is also very important.

In the setting of hypercalcemia, initial medical management includes intravenous fluids that promote the renal excretion of calcium. In the setting of hypervitaminosis D such as those in granulomatous disease, steroids are effective by inhibiting the effects of vitamin D.[2] In the setting of hypercalcemia of malignancy, treatment of the underlying cancer promotes a return to normal calcium levels. Bisphosphonates may also be used as medical management and potentially may inhibit osteoclast activity for up to one month. Calcitonin directly inhibits osteoclastic bone resorption and promotes the renal excretion of calcium by decreasing tubular reabsorption.

The milk-alkali syndrome is increasing in prevalence and should be considered in any presentation of hypercalcemia. Patients prophylactically taking calcium supplements or using over-the-counter antacids should be carefully monitored given their increased risk for hypercalcemia. ■

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