CLINICAL VIGNETTE

Hypercalcemia as the Initial Presentation of Lymphoma

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Case Presentation

A 70-year-old male with coronary artery disease and atrial fibrillation presented to urgent care with 3 days of abdominal discomfort, bloating and diarrhea. He reported onset of symptoms one day after eating chili. His abdominal discomfort localized around his umbilicus and was associated with loose stools. There was no melena or hematochezia and he reported prior intolerance of rich, spicy food and raw seafood. He denied any epigastric or right upper quadrant pain or fever. On exam his abdomen was soft and with localized tenderness around his umbilicus, without hernia, rebound or guarding. He was treated with simethicone and asked to limit intake of spicy foods. He continued to have abdominal discomfort despite simethicone and returned 4 days later. His loose stools resolved and he remained free of fevers, cramping, or melena. He had mild nausea but no vomiting. On repeat exam, he had normal bowel sounds and a soft non-distended abdomen with mild tenderness to palpation in the left upper quadrant. There also was a palpable mid abdominal bulge with easily appreciated pulsations. His calcium returned elevated at 12.8 mg/dL, and he was instructed to go to the emergency room. In the emergency room, additional history included absence of bone pain or weight loss, despite a decreased appetite, and presence of some night sweats for the past 3 days. His wife reported increased somnolence, sleeping more than 12 hours a day. He received normal saline hydration in the ER and was maintained on IV fluids and admitted. After hospital admission, he was found to have cervical lymphadenopathy as well as, a palpable umbilical nodule which may have explained the localized umbilical pain. The umbilical nodule was thought to be a Sister Mary Joseph lymph node which is associated with abdominal malignancy. Abdominal ultrasound demonstrated widespread lymphadenopathy, which was confirmed on CT neck/chest/abdomen/pelvis. Ultrasound guided core needle biopsy of the left neck nodule, showed malignant high-grade B-cell lymphoma. His PTH level was <2.5 and he received pamidronate to control his hypercalcemia. In addition, he developed new pancytopenia with hemoglobin of 12, platelet count of 60K, wbc 3.3k. Iron studies were consistent with anemia of chronic disease, likely secondary to lymphoma.

Discussion

One teaching point is patients with persistent symptoms that do not resolve after conservative measures warrant further evaluation to determine an etiology. Based on estimates from three prior studies, the frequency of diagnostic errors in the outpatient setting was estimated to be about 5% for US adults with half of these errors potentially harmful.[1] The National Academies of Sciences, Engineering, and Medicine (NAS) convened an expert committee to summarize what is known about diagnostic error and to propose recommendations to improve diagnosis.[2] They reported a plethora of reasons for diagnostic errors including inadequate collaboration and communication among clinicians, patients and their families and a health care system that is poorly designed to support the diagnostic process. Other factors include limited feedback about diagnostic performance and a culture that discourages transparency and disclosure of diagnostic errors, which may impede learning from these events and improve diagnosis.[2] The NAS expert committee developed multiple recommendations to improve diagnosis: 1) Facilitate more effective teamwork in the diagnostic process among health care professionals, patients, and families; 2) Enhance health care professional educational and training in the diagnostic process; 3) Ensure health information technology supports patients and health care professionals in the diagnostic process; 4) Develop approaches to identify, learn from and reduce diagnostic errors and near misses in clinical practice; 5) Establish a work system and culture that supports the diagnostic process and improvements in diagnostic performance; 6) Develop a reporting environment and medical liability system that facilitates improved diagnosis through learning from diagnostic errors and near misses; 7) Design a payment and care delivery environment that supports the diagnostic process; 8) Provide dedicated funding for research on the diagnostic process and diagnostic errors.[2]

Being aware of the frequency of diagnostic errors will allow providers to keep broader differential diagnoses to improve diagnostic accuracy and appropriate treatment. Patients may not present with all the typical signs of hypercalcemia or malignancy, but it is important to keep these in our differential.

The most common causes of hypercalcemia are hyperparathyroidism and malignancy, which account for around 80-90% of hypercalcemic states. Hyperparathyroidism accounts for most cases diagnosed in ambulatory populations and malignancy the most common cause in the hospitalized patients.[3] Our patient had symptoms of hypercalcemia with his abdominal pain and nausea, raising concern that given his symptoms, he was more likely to have a malignancy than hyperparathyroidism, which is usually asymptomatic. He admitted to lower

his calcium level and for an expedited work up of his hypercalcemia.

This patient's symptoms could be either from his hypercalcemia or his non-Hodgkin lymphoma as the two may overlap. Symptoms of non-Hodgkin lymphoma include lymphadenopathy and B symptoms of fever, night sweats, fatigue, weight loss, skin rash and pain.[4] Symptoms of hypercalcemia include mood changes, nausea, constipation, anorexia; polyuria, nephrolithiasis, acute and chronic renal insufficiency, cardiac arrhythmias, and muscle weakness.[5] This patient had abdominal discomfort and nausea as well as night sweats, anorexia and fatigue. These symptoms are associated with disease making it more difficult to identify the correct diagnosis.

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