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## CLINICAL VIGNETTE

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# Lambda Light Chain Myeloma Presenting with Asymptomatic Hypercalcemia

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### Case Presentation

A 54-year-old Caucasian woman with past medical history significant for bladder papilloma, IgA deficiency, melanoma, gastroesophageal reflux, nephrolithiasis, and renal cysts presented for evaluation of asymptomatic hypercalcemia for the past 2 months. She worked as a Financial Operations Manager for a large company and had a very healthy lifestyle. She exercised regularly and ate a low-fat diet consisting mainly of fruits and vegetables. She also took “Green Superfood Raw Reserve” and probiotic supplements on a daily basis but was otherwise not taking any medications.

She had recently been told by her primary care physician (PCP) that she had an elevated calcium level and was anemic. She was referred to a gastroenterologist who performed an esophagogastroduodenoscopy (EGD) and colonoscopy, which showed gastroesophageal reflux and internal hemorrhoids, respectively. No bleeding lesions were found. The patient went back to her PCP who referred her to the Emergency Room (ER) for further evaluation and treatment of her elevated calcium level. She went to her local ER and was discharged home without any treatment or further evaluation. Frustrated by this experience, she took it upon herself to find a reason for her elevated calcium and an online search revealed that an overactive parathyroid gland could be the answer. She subsequently scheduled an appointment with Endocrine Surgery for excision of a presumed parathyroid adenoma. Endocrine Surgery repeated labs, which showed an elevated calcium level of 12.5 mg/dL with a suppressed Intact PTH of 9 pg/mL. A 99mTc sestamibi scan did not show evidence of a parathyroid adenoma. She was then referred to Internal Medicine for further evaluation and treatment.

On physical exam, the patient was a thin, well-developed female with normal vital signs. Head and neck, pulmonary, cardiac, abdominal, and neurologic exams were normal. A repeat calcium level was elevated at 13.4 mg/dL. The patient was instructed to stop her herbal supplements and return to clinic in one week for repeat labs. One week later, her calcium and corrected ionized calcium came back elevated at 12.6 mg/dL and 1.57 mmol/L, respectively. Basic metabolic panel, including anion gap, was otherwise normal. Complete blood count was notable for a hemoglobin of 9.9 g/dL with a mean corpuscular volume of 91.8 fL. Anemia workup revealed low iron at 17 mcg/dL, Vitamin B12 that was low normal at 279 pg/mL, and folate that was slightly low at 8.0 ng/mL. Serum protein electrophoresis (SPEP) showed

decreased total protein with reduced alpha and gamma fraction without monoclonal bands. Urine protein electrophoresis (UPEP) revealed a monoclonal band present in the gamma region with an M-protein of 61.6%. Serum immunoglobulin levels returned with a marked elevation in free lambda light chain at 1135 mg/L (normal range 5.7 to 26.3 mg/L) with a kappa/lambda ratio of 0.01. Bone marrow biopsy confirmed Multiple Myeloma with plasma cells comprising 40% of the marrow. As such, the patient was diagnosed with Lambda Light Chain Myeloma and started on a clinical trial regimen of Lenalidomide (Revlimid), Dexamethasone, and Elotuzumab. The patient is now 14 months from diagnosis and remains on the same treatment regimen. She is responding well to treatment with resolution of hypercalcemia and anemia.

### Discussion

Hypercalcemia is a common clinical problem that is encountered in the primary care setting. It is the result of increased bone resorption, excessive gastrointestinal absorption, or decreased renal excretion of calcium. The most common causes for hypercalcemia are hyperparathyroidism and malignancy which account for over 90% of cases.<sup>1</sup> Hypercalcemia in primary hyperparathyroidism is due to parathyroid hormone (PTH) mediated activation of osteoclasts leading to increased bone resorption. In contrast, the mechanism of hypercalcemia in malignancy depends upon the cancer.

Malignancy should be suspected in a patient with hypercalcemia and a suppressed PTH. Osteolytic lesions account for about 20% of cases of hypercalcemia of malignancy.<sup>2</sup> Induction of local osteolysis of tumor cells is common with solid tumors metastatic to bone and with multiple myeloma. It is less common in lymphoma and leukemia.

Multiple myeloma is characterized by the neoplastic proliferation of plasma cells derived from B cells producing a monoclonal immunoglobulin. They proliferate in the bone marrow and can cause skeletal destruction leading to osteolytic lesions and/or pathologic fractures. Hypercalcemia in multiple myeloma patients may also be the result of the monoclonal protein binding calcium.<sup>3</sup> Hypercalcemia with a calcium level of  $\geq 11$  mg/dL was found in only 13% of patients with multiple myeloma at the time of diagnosis and can

require emergent treatment. In the same series of patients, anemia was found in 73%.<sup>4</sup>

The diagnosis of multiple myeloma requires that the bone marrow plasma cell percentage be greater than or equal to 10% or have biopsy-proven bony or soft tissue plasmacytoma. In addition, the presence of related organ or tissue impairment of a biomarker associated with near inevitable progression to end-organ damage is required to fulfill the diagnostic criterion per the International Myeloma Working Group.<sup>5</sup> In this case, our patient met diagnostic criteria with a bone marrow plasma cell percentage of 40% and had related organ impairment as evidenced by her anemia and hypercalcemia. This case reminds us that asymptomatic hypercalcemia that is confirmed with a repeat calcium requires further evaluation, and once hyperparathyroidism has been ruled out, malignancy remains at the top of the differential.

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