

A case report: hypercalcemia due to vitamin supplementation in a patient with neurofibromatosis

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Summary

A 54-year-old female with history of neurofibromatosis who presented with severe hypercalcemia and renal failure secondary to over supplementation of calcium and vitamin D.

KEY WORDS: vitamin D overdose; hypercalcemia; vitamin D supplementation; calcium supplementation.

A 54-year-old female with history of neurofibromatosis, breast cancer with lumpectomy, chemotherapy and arimidex, calcific tendonitis, resected brain tumor and osteoporosis presented to clinic with four weeks of fatigue, reduced exercise tolerance, exertional chest pain, mental slowness, shortness of breath, constipation and disequilibrium. Patient described longstanding constipation for which she occasionally takes miralax and an intentional weight loss of 10 lbs. Patient also reported an illness one month prior with a dry cough. She reported some minor nausea, but denied vomiting, anorexia, abdominal pain, black or bloody stools and had a negative hemocult test prior to presentation. Home medications include anastrozole (arimidex), topiramate and supplements consisting of kirkland signature calcium citrate tablets (500mg calcium, 800 IU vitamin D3) four times a day, 2,000 IU of vitamin D3 twice per day, Targets Women's Health Vitamin once per day (250% DV vitamin D, 50% DV calcium), and reports drinking one glass of milk a day and eating one yogurt, but no other sources of calcium. Without including the milk and yogurt values, the patient was taking 2600mg of calcium and 8,700IU of vitamin D3 per day. Physical exam notable only for numerous neurofibromas, but was otherwise unremarkable. Laboratory testing revealed calcium level of 17.1mg/dL (Ref. 8.5-10.3), Hgb of 9.8g/dL (Ref. 11.5-15.0), creatinine 3.44mg/dL, BUN 51 mg/dL, GFR of 14, magnesium of 3.1 mg/dL (Ref. 1.7-2.3). ECG was significant for widened QRS and bradycardia. Patient was admitted for aggressive intravenous fluids, calcitonin, and further work up, with current medications and supplements stopped, no diuretics were started due to acute kidney injury. During the course of a 3 day hospital stay, calcium levels de-

creased to 13.8mg/dL (1 day), 10.7mg/dL (2 days), and 9.8mg/dL on day 3. IV fluids were stopped on day 2 due to lower calcium levels, and the development of peripheral edema, shortness of breath and worsening anemia. Hemoglobin levels decreased steadily during the hospital stay, 8.4g/dL (1 day), 7.1g/dL (2 days), 6.8g/dL on day 3, requiring a transfusion of 1 unit of blood on day 3. Laboratory tests ordered on intake revealed normal WBC, liver enzymes, lipase, troponin, LDH, TSH, vitamin B12, Iron, TIBC, ferritin, urinalysis, serum protein electrophoresis and serum immunoelectrophoresis. Reticulocytes were within normal limits (0.93, normal range 0.7-2.5) and parathyroid hormone (14 pg/mL, normal range 10-65 pg/mL - with a calcium of 15.2 mg/dL at draw), magnesium 2.6mg/dL (high normal 1.7-2.3). Lab tests were positive for elevated Kappa light chains with normal Lambda light chains with a 2:1 ratio. Ultrasound and chest X-ray revealed no abnormalities, and osseous survey revealed no lytic lesions. Patient was stable for discharge on day 3 after receiving one unit of blood, labs were ordered for Vitamin D, ACE and parathyroid related protein, and patient underwent bone marrow biopsy just before discharge.

After discharge, calcium levels remained stable with 9.5mg/dL at 1 week after admission and 10.3mg/dL at 1 month and 2 months. Patient remained asymptomatic with no exercise intolerance. Anemia remained stable with hemoglobin of 9.7g/dL at 1 week and 10.0 after 1 month. Kidney function improved, with a creatinine of 1.02 mg/dL and GFR of 56 after 2 months. Laboratory tests post hospitalization revealed normal parathyroid related protein, normal angiotensin converting enzyme, normal vitamin D 25 (55 ng/mL Ref. 20-79 ng/mL) and low vitamin D 1,25 (<0.08, Ref. 18-72 - pg/mL) likely related to hydration and renal failure. Bone marrow biopsy showed no cytogenetic, flow cytometry or pathologic abnormalities and no osseous metastatic disease on whole body scan. Brain MRI, as follow up to post resection MRI from 2014, showed postoperative changes from right frontal tumor resection without evidence of recurrence, no new findings, normal appearing pituitary and parasellar regions. The patient continues to do well with no recurrent or new symptoms, recently completing a hiking trip in the mountains.

For most clinicians, a patient presenting with hypercalcemia, anemia and renal failure automatically prompts the diagnosis of multiple myeloma (MM). However, work up for MM was diffusely negative, with the elevated serum light chains more consistent with renal failure than MM. Workup for other malignancies also yielded no positive results, and her renal failure and anemia have improved with the correction of the hypercalcemia, leading to a presumptive diagnosis of vitamin overdose. Unfortunately, vitamin D levels were not assessed until after the patient's calcium levels had significantly declined and the patient had received large amounts of IV fluids. Parathyroid hormone levels remained within normal limits after discharge excluding the common cause of hyperparathyroidism. However, the lack of any other diagnosis, steady state after discharge and large amount of daily vitamins support our working diagnosis of over supplementation of vitamins.

Presented here is a case of severe hypercalcemia caused by increased intake of calcium and vitamin D at a previously unreported level. Most reported instances of hypercalcemia caused by high levels of vitamin intake usually caused mild hypercalcemia and is associated with much higher levels of intake (1-4). As patients currently continue to take increasing numbers of supplements, it is important for clinicians to be aware of possible complications, especially as supplements are not regulated and thus levels can vary from what is labeled on the bottle, such as increased vitamin D levels found in hypercalcemic patients related to increased dairy supplementation (5). As no home testing was performed with this patient, we can not rule out the possibility of increased dosing due to manufacturing error. More importantly, a recent report showed that the prevalence of vitamin D and calcium deficiency in the United States has been vastly overestimated, with 97% of the population receiving adequate levels (6). Thus, despite dose response curves showing inconsistent responses and lacking clear relationships, it is important for clinicians to monitor levels of supplements taken at home (3). Specifically in this case, the patient was taking these supplements at the guidance of her physician, despite the fact that the levels exceed the recommended daily levels and the point at which the risk of harm starts to increase (4000 IU/day) (6).

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