CLINICAL VIGNETTE

Acute and Chronic Kidney Injury Associated with Vitamin D Toxicity

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Case Report

A 76-year-old female presents to her primary physician for annual wellness visit. Her previous medical history was remarkable for anxiety and remote history of nephrolithiasis, without prior hospitalization. She was self-medicating with vitamin supplements including multivitamin one tablet a day and Vitamin D 4000IU a day. Her laboratory tests after the visit revealed elevated creatinine of 6.7 mg/dL; serum potassium of 6.5 mmol/L; and total serum calcium of 15.7 mg/with ionized calcium of 15.8. She was admitted to hospital and evaluation of hypercalcemia initiated. Review of records found elevated serum calcium of 10.7 mg/dL and serum creatinine of 0.9 mg/dL two years prior to her hospitalization.

Patient's evaluation for hypercalcemia included normal serum and urine immune electrophoresis; PTH 25, normal PTHrp level; elevated phosphorous of 7.8 mg/dL; elevated vitamin D,25 (OH) > 150pg/mL; and elevated vitamin D,1,25-Di(OH) of 180 pg./mL. Ultrasound of kidney and bladder showed bilateral nephrolithiasis and nephrocalcinosis. A diagnosis of hypercalcemia due to vitamin D toxicity was made. Her kidney injury was related to nephrolithiasis and nephrocalcinosis secondary to prolonged hypercalcemia. She was treated with intravenous, normal saline, along with furosemide and denosumab. She was discharged from hospital after 6 days with her serum creatinine and serum calcium were 3.6 mg/dL and 10.7 mg/dL on the day of discharge. Patient was seen for renal follow up two weeks after discharge. She was asymptomatic with normal physical examination except for mild anxiety. Laboratory tests showed improvement in renal function with serum creatinine of 2.55 mg/dL. 25 OH Vitamin D remained above 100/g/mL showed elevated vitamin D,25 (OH) of > 150 pg./mL; and elevated vitamin D,1,25-Di(OH) of 180pg/mL. Her calcium remained elevated at 11.8 mg/dL with ionized calcium of 1.48 mmol/L.

She was referred to endocrine for further evaluation and treatment of her persistent hypercalcemia.

Discussion

Hypercalcemia is an etiology of chronic and acute kidney injuries by itself regardless of its underlying cause. There are many causes of hypercalcemia including hypervataminosis D.[1] Elevated serum vitamin D level could be due to over consumption of vitamin D,[2] like our case, or due to excess production of endogenous vitamin D,1, 25-Di(OH) by conversion of vitamin D, 25-(OH) to vitamin D, 1, 25-Di(OH).[3] Another rare mechanism of high serum vitamin D level is gene mutation encoding vitamin D 24 hydroxylase that degrades both vitamin D, 25-(OH) and vitamin D,1,25,Di(OH) into their inactive metabolites.[4]

Prolonged hypercalcemia results in prolonged hypercalciuria that in turn result in chronic kidney injury through nephrocalcinosis and nephrolithiasis.[5] Hypercalcemia can acutely reduce blood flow to the kidney by vasoconstriction of afferent arterioles in the kidney which can lead to acute kidney injury through prerenal azotemia that can progress into acute tubular necrosis.[6] Due to hypercalcemia, patients develop diabetes insipidus that is associated with volume depletion and dehydration, that can result in hypoperfusion of the kidney, which enhances prerenal azotemia and acute kidney injury.[7]

Use of Vitamin D supplements with and without calcium have widespread use to prevent osteoporosis in patients without risk factors despite of its controversial benefit.[8] Vitamin D supplement is also prescribed in patients with reduced renal function to prevent bone disease associated with vitamin D deficiency in this group of patients.[9] Clinicians should closely monitor their patients' serum and urine calcium level to prevent hypercalciuria, and hypercalcemia while patients are on these supplements to prevent chronic and acute kidney injury.

Vitamin D supplement in patients with mild to moderate reduced renal function due to any underlying kidney disease could be a challenge. Hypercalcemia due to high level of vitamin D can result in acute kidney injury.[10] This acute kidney injury can result in irreversible damage to an already abnormal renal tissue and can result in lower baseline renal function.

Patients with hypercalcemia deserve a complete evaluation for the cause of hypercalcemia. Hypercalcemia could be the red flag to diagnoses such as lymphoma,[11] granulomatous diseases, sarcoidosis,[12] and paraneoplastic manifestation of malignancies, lung cancer,[13] multiple myeloma, or abnormalities of vitamin D metabolism.

Persistent hypercalcemia and elevated vitamin D,25-(OH) and vitamin D1,25-Di(OH) after two weeks of discontinuation of vitamin D supplements warrants further investigation for the cause of hypercalcemia. Although prolonged half-life of

vitamin D, 25 (OH),[2] makes the elevated vitamin D level as the more likely cause of this patient's hypercalcemia.

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