Too Much of A Good Thing: A Case of Suspected Acute Tubular Necrosis Provoked by Hypervitaminosis D

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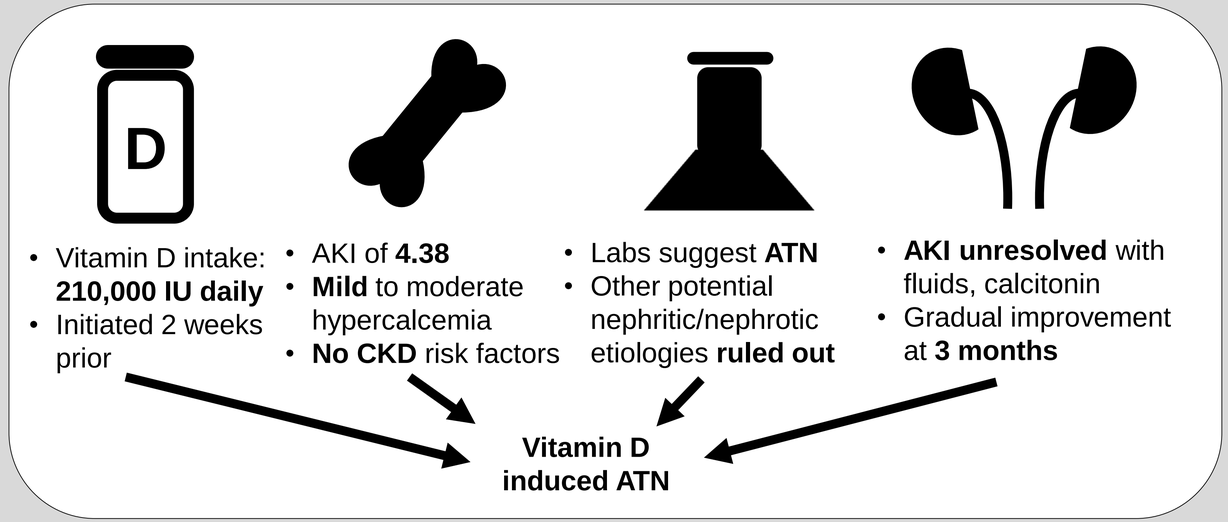
Introduction

- Calcitriol is a vitamin critical in regulating calcium homeostasis, maintenance of musculoskeletal integrity, and both a commonly prescribed medication and over the counter supplement.
- However, the incidence of vitamin D toxicity is escalating, manifesting clinically with confusion, polyuria, polydipsia, muscle weakness, and nausea and vomiting (1).
- While acute hypercalcemia, especially in the setting of milk-alkali syndrome, has been demonstrated to induce a reversible AKI, the direct cytotoxic effect of excess Vitamin D on the renal parenchyma in the setting of lower levels of serum calcium, has not been well studied nor documented.

Case Presentation

- A 62-year-old male presented to the ED after outpatient screening labs revealed a **creatinine of 2.66** mg/dL and **calcium of 13.2 mg/dL** two days prior.
- PMH was significant only for chronic chest pain, with cardiac catheterization at a later date revealing normal coronaries and ejection fraction.
- Patient admitted no symptoms other than some polyuria, condoned drinking adequate fluids, and eating regularly.
- Physical exam was largely normal, save an elevated blood pressure to 149/116.
- While he admitted to no medications other than melatonin, his supplements included a daily serving of **oral vitamin D**, which he purchased in a wholesale powdered form 1-2 weeks ago.
- His daily intake was calculated to be **210,000 IU, or 5,250 mcg of calcitriol daily (tolerable upper intake level 4000 IU or 100 mcg).**



Hospital Course

- Repeat labs on admission revealed a creatinine of 4.38 mg/dL, BUN of 52 mg/dL, and calcium of 13.6 mg/dL, with other labs within normal limits.
- Nephrology was consulted, and prerenal measures were initiated with aggressive fluid resuscitation.
- Workup for hypercalcemia/intrinsic kidney pathologies was negative for protein electrophoresis, urine light chains, urinalysis, and TSH, with an appropriately suppressed parathyroid response.
- CT imaging was noncontributory of any obstructive/structural pathology.
- 25-Hydroxy and 1,25-Dihydroxy Vitamin D were elevated beyond the measuring capabilities of the lab at >480 ng/mL and >600 pg/mL respectively.
- Fractional excretion of sodium was calculated to be 2.3%, BUN;Cr ratio of 12.9, urine sodium of 57 mmol/L, with a creatinine rise of rate ~0.86/mg/dL/day.
- Despite several days of continuous IV fluids at 150 cc/hr of NS, in addition to calcitonin treatment, creatinine improved only to 2.96 mg/dL by discharge on day 3 of hospitalization, with calcium normalized to 9.8 mg/dL..
- At follow up 3 months later, creatinine was still elevated above his baseline, at 1.6 mg/dL, despite a now normal calcium level and cessation of all supplements.

Discussion

- Hypercalcemic AKI, even at levels as high as 19.9 mg/dL, typically resolves with treatment by day 11; this patient failed to resolve, suggesting additional insult.
- In calcitriol-induced AKI, toxicity of excess free Vitamin D metabolites exceeds the capacity of neutralizing vitamin D binding proteins (3).
- In vitro, calcitriol potentiates ATP depletion, and cytotoxicity of renal tubular cells even in the absence of hypercalcemia (4).
- In vivo, excess calcitriol exacerbates cellular azotemia 2-3 times, even with modest hypercalcemia (4).
- A similar cohort of patients demonstrated time to recovery of baseline kidney function of up to 3 months (5).
- A similar case reported tubular atrophy, interstitial fibrosis on biopsy, and a two-year duration for full recovery of baseline kidney function (6).
- Given the exclusion of other causes, a single inciting factor shortly before his presentation, and a clinical course consistent with similar cases, this patient may present a rare case of vitamin D induced ATN.
- Further study is needed to better elucidate this novel pathology, especially as supplement induced toxicities continue to become more prevalent.

References

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