ABSTRACT

Vitamin D deficiency is widely prevalent across the globe. This has lead to widespread use of vitamin D supplements in populations. We present our experience of vitamin D toxicity in a subject resulting in hypercalcemia and CHB (Complete Heart Block). A 70-year-old female, known hypertensive for thirty five years and diabetic for seven years underwent total knee replacement (TKR) for osteoarthritis left knee in December 2010. For perioperative glycemic control, multiple subcutaneous injections of insulin were advised. Patient later presented with poor glycemic control, decreased appetite and constipation for last 1 month with history of episodes of transient loss of consciousness for 15 days and recurrent vomiting. Biochemical work-up showed hypercalcemia (Serum calcium 12.4 mg/dL). Sr. albumin, ALP, Sr. phosphorus and PTH levels were normal, thus suggesting PTH independent hypercalcemia. Strong suspicion led us to check vitamin D levels in dilution which were 2016 ng/mL, thus confirming vitamin D toxicity. Retrospective analysis of treatment history revealed patient receiving 4 injections of Architol (6 Lac units im) prior to presentation. Work-up for malignancy was negative, brain imaging and EEG were normal. Holter was suggestive of intermittent CHB. Patient was given hydration, injection calcitonin 100 I.U. subcutaneously, injection pamidronate 60 mg infusion, with serum calcium levels normalizing, with relief in constipation, vomiting and behavioral improvement. However, persistence of rhythm disturbances led to permanent pacemaker placement. The present case highlights the dangers of indiscriminate vitamin D usage, exposing patients to potentially life threatening complications.

Key words: Vitamin D toxicity, hypercalcemia, complete heart block

INTRODUCTION

Vitamin D deficiency is widely prevalent across the globe (1). Whereas the skeletal role of vitamin D is clearly known, evidence is mounting that vitamin D has extra-skeletal benefits.

Vitamin D deficiency and insufficiency have been defined as serum 25 (OH)D of less than 20 ng/ml and 21-29 ng/ml, respectively. Recent epidemiological data document the high prevalence of vitamin D in all age groups, across the world.40 to 100% of U.S. and European elderly men and women living in the community (not in nursing homes) are deficient in vitamin D. Similar results have been reported from India. In School based study of 5,137 apparently healthy children, aged 10-18 years, vitamin D deficiency was seen in 93% in lower socioeconomic and 85% in upper socioeconomic group children. When 50 patients (mean age, 62.2 ± 12.3 years) with fragility hip fractures were assessed, vitamin D deficiency was observed in 96.7 %. Recently voluminous data has emerged on association of vitamin D deficiency with many chronic diseases. The antiproliferative, prodifferentiative, and immunomodulatory actions of vitamin D are being investigated for the potential treatment of many pathologic conditions including psoriasis, type 1 diabetes mellitus, rheumatoid arthritis, multiple sclerosis, hypertension, CAD, and many cancers.
This has produced an epidemic of apparent vitamin D deficiency, leading to widespread use of vitamin D supplements in populations in whom benefits have yet to be demonstrated by randomized, controlled trials.

We present our experience of vitamin D toxicity in a subject resulting in hypercalcemia and CHB

**Case Report**

A 70-year-old female, known hypertensive for thirty five years and diabetic for seven years underwent total knee replacement for osteoarthritis left knee in December 2010. For perioperative glycemic control, we started multiple subcutaneous injections of insulin and discharged on same with good glycemic control.

Patient consulted us again in February 2011 (2 months later), with poor glycemic control, decreased appetite and constipation for last 1 month. There was history of episodes of transient loss of consciousness for 15 days and recurrent vomiting. Each episode of loss of consciousness occurred around meal time (30 min after injecting regular insulin, however blood glucose was never checked to confirm hypoglycemia). Relatives also noticed behavioral changes in patient in terms of increased irritability, minimal social interaction and lack of sleep. Clinical examination was unremarkable except for mild dehydration.

On biochemical evaluation, the biochemical profile and serial ECGs were within normal limits except serum Calcium of 12.4 mg/dl. The corresponding serum phosphorus, serum albumin, serum alkaline phosphatase values 3.6 mg/dl, 3.6 gm/dl and 154 I.U., respectively. Records of the early post-operative period were not suggestive of any hypercalcemia.

Initially hypercalcemia was thought to be due to dehydration, however a decision to send repeat calcium along with serum PTH. Serum calcium was 12.4 mg% with corresponding serum PTH value of 12.17 pg/ml. Thus, it was a case of PTH independent hypercalcemia. In view of serum 25 OH vitamin D levels more than 120 ng/ml, we kept the possibility of vitamin D toxicity and repeated serum 25 OH vitamin D levels by dilution, which came as high as 2016 ng/ml.

Review of past treatment revealed that patient had received 4 injections of Arachitol 6 lac units each over a period of few weeks (total dose 24 Lac units) in January for complaints of generalized weakness.

Work-up for malignancy was negative, brain imaging and EEG was normal. Patient was started on anti-depressants after psychiatry opinion. Holter was suggestive of intermittent CHB (Complete Heart Block) and patient was considered for temporary pacemaker insertion.

Patient was given hydration, under hemodynamic monitoring and injection Calcitonin100 I.U. subcutaneously and injection Pamidronate 60 mg infusion, with serum calcium levels coming down to 8.8 gm%, and relief in constipation, vomiting and behavioral improvement.

However, persistence of rhythm disturbance, despite resolution of hypercalcemia, permanent pacemaker was implanted.

Patient was discharged in march 2011 and was advised adequate hydration, however she was admitted again in May 2011 with recurrent vomiting, serum calcium levels of 11 mg% and serum 25 OH vitamin D level (by dilution): 880 ng/ml. Patient was managed with intravenous hydration and injection Calcitonin.

**Discussion**

In the present case, patient was given multiple injections of vitamin D for the complaints of generalized body aches without any documentation of serum vitamin D deficiency.

Also, with availability of oral vitamin D preparations, intramuscular preparations do not offer any advantage unless severe malabsorption is present. As Vitamin D is stored in fat, toxicity once occurs, takes a very long and unpredictable time to resolve. As in our case, patient initially improved with supportive treatment but presented again with symptoms of hypercalcemia.

As vitamin D preparations are available over the counter, and the concept of “vitamin D deficiency” becoming widespread, this is a matter of concern. If we do not become vigilant now, it will not be a surprise to see more and more cases of vitamin D toxicity in near future, with many cases going undiagnosed and unreported.

Koul et al., reported ten cases of hypercalcemia due to vitamin D intoxication in a case series from Kashmir valley. Khadgawat et al., reported acute vitamin D toxicity in 8 months old child who received 3 injections of Arachitol 6,00,000 units each and presented with symptomatic hypercalcemia and bilateral medullary nephrocalcinosis.

As per the Endocrine Society Clinical Practice Guideline for the treatment of vitamin D deficiency, vitamin D supplementation beyond recommended daily needs to
prevent cardiovascular disease or death or improving quality of life is not recommended. Also, there are specific recommended dietary allowances for vitamin D for each age group and specific doses to treat vitamin D deficiency for each age group based on safety data. For a 70-year-old female, RDA of 600 I.U. of vitamin D has been advocated, 4000 IU per day being the upper limit.

The present case was given 24 lac IU vitamin D over 30 days (four injections of Arachitol, 6 lac IU each), which comes to 80,000 IU per day. This resulted in serum 25 OH D levels of 2,016 ng/ml. Levels above which vitamin D toxicity occurs has been described are 150 ng/ml\(^{11}\). An upper limit of 10,000 IU/d of vitamin D for adults has been described safe.

Thus, vitamin D deficiency, although common, needs to be treated with caution and inadvertent use of vitamin D supplements be avoided.

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