



Case Report

An Unusual Case of Persistent Vomiting due to Iatrogenic Hypervitaminosis D

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ABSTRACT

65-year-old postmenopausal woman presented with persistent vomiting as a result of iatrogenic hypervitaminosis D. She was treated with intravenous fluid, diuretics and calcitonin with clinical improvement and biochemical recovery. We recommend that a diagnosis of overdose of vitamin D should be suspected in any patient presenting with persistent vomiting and hypercalcemia, particularly in the presence of normal parathyroid hormone. Its prompt treatment alleviates symptoms and prevents ongoing acute kidney injury.

Keywords: Hypervitaminosis; Vitamin D Toxicity; Adverse drug reaction; Iatrogenic hypervitaminosis D; Iatrogenic emesis

INTRODUCTION

Vitamin D is a prohormone which plays an important role in calcium homeostasis and bone mineral metabolism as well as subserves in a wide range of fundamental biological functions like cell differentiation, cell growth inhibition as well as immune modulation. Vitamin D deficiency leads to a mineralization defect in the skeleton and enhances mobilization of calcium from the skeleton resulting in porotic bone. Although no minimum daily dietary intake of vitamin D has been identified, for adults exposed to ample sunlight less than 2.0µg/day (that is 80 units/day) of dietary intake is associated with its overt deficiency in adults. Sun exposure and use of fortified or enriched foods are the methods by which mild

vitamin D deficiency can be corrected. Moderate to severe vitamin D deficiency can be treated by oral administration of pharmacological dose of vitamin D 50,000IU/week for 6- 8 weeks. [1] Due to a wide therapeutic index, vitamin D toxicity is extremely rare. However it does occur at excessively high doses. We present here a classic case of iatrogenic hypervitaminosis D which presented with persistent vomiting, hypercalcemia and azotemia (Acute renal failure)

CASE PRESENTATION

65-years old postmenopausal woman presented with history of recurrent vomiting, pain in abdomen, anorexia and constipation for two months. There was no history of

fever, headache, cough, shortness of breath or urinary symptoms. She was known case of low backache and osteoporosis for which she was on treatment with oral vitamin D3 and calcium carbonate along with symptomatic analgesic for last five years

On physical examination, she was conscious and well oriented. There was no pallor, icterus, significant lymphadenopathy, pedal edema or dyspnoea. She was afebrile and JVP was normal. Blood pressure - 130/80mmHg, pulse- 84/minute and respiratory rate- 20/minute. Systemic exam revealed no abnormality. Laboratory investigations revealed hemoglobin 12gm%, white blood cell count $10 \times 10^3/\text{mm}^3$, platelet count $250000/\text{mm}^3$, blood urea nitrogen (BUN) 60mg/dL, creatinine 3.1mg/dL, sodium 138mEq/L, potassium 3.9mEq/L, serum calcium 12.55mEq/L, phosphorous 3.0mEq/L, serum bilirubin 0.80mg/dL, protein 6.0g/dL, albumin 3.8g/dL, globulin 2.5g/dL, alanine transaminase 26IU/L, aspartate transaminase 30IU/L, alkaline phosphatase 56IU/L and erythrocyte sedimentation rate 46mm. Mantoux test was negative and parathyroid hormone was 11.50pg/mL(normal limit). Urinalysis and microscopic exam were normal. Urine for Bence Jones protein was negative. Chest X-ray and electrocardiogram were within normal limit. An ultrasound of abdomen was normal. An ultrasound of neck did not reveal any parathyroid mass. High-resolution computed tomography of her chest and magnetic resonance imaging of her brain were also essentially normal. Hence the biochemical evaluation revealed only raised BUN and serum creatinine suggesting acute renal failure with hypercalcemia, in the absence of evidence of chronic kidney disease, multiple myeloma or hyperparathyroidism. A detailed history of previous treatment revealed that she had received an injection of Arachitol (vitamin D3) 600,000IU

intramuscular every alternate day for 07 doses by local registered medical practitioner for osteoporosis and low backache .

Her serum 25-hydroxyvitamin D [25(OH)D] level was 155ng/mL which was in the toxic range (normal 20 to 30ng/mL) and a diagnosis of vitamin D toxicity induced acute kidney injury and hypercalcemia was established. To rule out chronic kidney disease an ultrasound for kidneys and routine urine microscopy were ordered, which were normal. For hypercalcemia, she was treated with intravenous fluid, diuretics and calcitonin and had clinical improvement. Her serum calcium and creatinine levels were monitored regularly; these gradually declined to normal levels in the next 15 days. She was discharged with a prescription of calcium restricted diet along with good hydration and she is doing well.

DISCUSSION

This was a classic case of iatrogenic hypervitaminosis D which presented with persistent vomiting and acute renal failure. Hypervitaminosis D can occur when pharmaceutical vitamin D is taken in excess as it happened in our case. The manifestation could be related to hypercalcemia and or acute kidney injury.^[2]

The biologically active metabolite of vitamin D, 1,25-dihydroxyvitamin D₃, affects mineral homeostasis and has numerous other diverse physiologic functions including effects on growth of cancer cells and protection against some immune disorders.^[3]

Vitamin D deficiency can be treated with oral administration of a pharmacological dose of vitamin D 50,000IU/week for 6 to 8 weeks.^[1] Even though vitamin D toxicity is extremely rare, due to the wide therapeutic index, it does occur at excessively high doses. The

guidelines of the Food and Nutrition Board of the USA specify 2000IU as the highest vitamin D intake that healthy adults can consume daily without risk of hypercalcemia.^[4] However, these patients should be monitored by periodic estimation of 24-hour urinary calcium excretion, which should not exceed 250mg. Very little is known about the mechanism of vitamin D toxicity.^[5] The lipophilic nature of vitamin D explains its adipose tissue distribution and its slow turnover in the body (half-life approximately 2 months), whereas its main transported metabolite, 25-hydroxyvitamin D3 [25(OH)D3], has a half life of approximately 15 days. Although current data support the viewpoint that the biomarker plasma 25(OH)D3 concentration must rise above 750nmol/L to produce vitamin D toxicity, the more prudent upper limit of 250nmol/L might be retained to ensure a wide safety margin. There also is evidence that despite the current heavy reliance on serum 25(OH)D3 concentration for the diagnosis of an individual's vitamin D status, local tissue vitamin D intoxication may be present in individuals with much lower serum 25(OH)D3 concentrations than are currently appreciated.^[5] An individual's serum 25(OH)D3 concentration may appear to be "low" for reasons totally independent of sunlight exposure or vitamin D intake. Serum 25(OH)D3 concentration is only poorly responsive to increases in vitamin D intake and the prolonged routine consumption of thousands of international units of vitamin D may interfere with the regulation of phosphate homeostasis by fibroblast growth factor-23 and the Klotho gene product with consequences that are detrimental to human health.^[5]

Clinical manifestations of vitamin D toxicity include hypercalcemia, hypercalciuria, kidney stones, hyperphosphatemia, polyuria, polydipsia, ectopic calcification of soft tissues (kidney

and lung), nausea, vomiting, anorexia, constipation, headache and hypertension.^[6,7] In a recent paper Pandita *et al*^[8] reported a case series of 15 patients (most of them elderly) with iatrogenic symptomatic hypercalcemia in whom toxicity occurred due to empirical excessive administration of vitamin D by oral and parenteral route. In another case series by Koul *et al*,^[9] 10 cases of hypercalcemia due to vitamin D intoxication were reported with features of vomiting, polyuria, polydipsia, encephalopathy and renal dysfunction. All the patients had demonstrable hypercalcemia and vitamin D levels were high in nine of the 10 cases. The patients had received high doses of vitamin D and no other cause of hypercalcemia was identified. Treatment of hypercalcemia resulted in clinical recovery in nine cases.^[9]

CONCLUSION

Thus we conclude that if a patient presents with persistent vomiting and hypercalcemia particularly in the presence of normal parathyroid hormone, then a diagnosis of overdose of vitamin D should be suspected because its correction not only alleviates symptoms but can also prevent acute kidney injury.

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