


Redundancy Is of No Good; Iatrogenic Hypervitaminosis D: A Rare Case of Persistent Vomiting Due to Hypercalcemia

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ABSTRACT

INTRODUCTION: Iatrogenic or physician-induced hypervitaminosis D is a rare cause of persistent vomiting. To the best of our knowledge, this is the first case report on iatrogenic hypervitaminosis D presenting with persistent vomiting in Pakistan.

CASE REPORT: We report a rare case of continual vomiting for 15 days in a 48-year-old woman of Pakistani descent. She was a known case of diabetes mellitus for 8 years, which was well controlled at the time of presentation.

CONCLUSIONS: The correct diagnosis of our patient was based on clinical suspicion, appropriate lab tests, and deliberation of the differential diagnosis. It is important to consider hypervitaminosis D as a cause of persistent vomiting if no other obvious is apparent.

KEYWORDS: calcidiol, vitamin D, iatrogenic disease, vomiting

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Introduction

Vitamin D, also known as calcidiol, is an important fat-soluble vitamin and pro-hormone responsible for a wide array of body processes, especially the metabolism of calcium and mineralization of bone, with functions such as cell differentiation, growth inhibition, and cell modulation still a process of evolution.

Toxicities of vitamins are rare occurrence as it is an essential biological component. Hypervitaminosis D usually results from increased therapeutic doses, high dietary intake, or highly fortified food with vitamin D and unsupervised supplementation. The increase in 1,25-OHD levels associated with sarcoidosis is secondary to increased CYP27B1 (1 α -hydroxylase) enzyme activity.¹ Clinical presentation of hypervitaminosis D includes lethargy, confusion, constipation, nausea, and anorexia; however, the most notable signs of hypervitaminosis D are hypercalcemia and hypercalciuria.² Appearance of such symptoms is mainly due to elevated serum levels of calcium as a result of vitamin D toxicity.³

We highlighted here a case of physician-induced hypervitaminosis D, which presented with repeated vomiting. Such case reports are seldom found in medical literature.

Case Presentation

A 48-year-old woman, known case of diabetes mellitus for 8 years, on oral hypoglycemics with a well-controlled blood sugar, presented with the complaint of vomiting for 15 days, for which she went to various local GPs and hospitals but, she did

not get any relief. Detailed workup was done to exclude possible causes like infectious, metabolic, drug-induced, or any other potential cause. Her vomiting was characterized by 2 to 3 episodes per day, non-projectile, without any blood, bile, or foul-smelling content (like undigested food). She also had a history of back pain for 6 years that aggravates on activity and numbness in feet. She also had a history of abdominal pain, polyuria, and polydipsia. She also gave the history of receiving multiple injections for back pain by some local physician in her residential area. On further investigation, it was found that she received vitamin D supplements 15 000 $\mu\text{g}/\text{d}$ (equivalent to 600 000 IU/d) IM for 6 consecutive days a month back.

She is a known case of type 2 diabetes mellitus since 8 years, which was well-controlled with metformin; other than that, her past medical, surgical, and blood transfusion history was not significant.

Examination

On examination, she was conscious and oriented. Her vitals were BP was 130/70 mmHg, pulse was 76 beats per minute, respiratory rate was 15 breaths per minute, and temperature was 98°F. Pallor, edema, and icterus were absent. No significant clinical findings were found in her respiratory, abdominal, and cardiovascular examinations. However, her central nervous system examination displayed a mild impairment in touch, pain, and vibration on the right side along with decreased pulsations of dorsalis pedis artery on the right side while there were



diminished reflexes in both lower limbs. All the other common causes of long-term vomiting were excluded on the basis of clinical examination and lab findings.

Lab findings

Complete blood count reports showed hemoglobin of 11.8 g/dL with mean corpuscular volume (MCV) of 73 fL, but with normal white cells and platelet count. Blood biochemistry showed Serum Lipase of 17.7 U/L (normal=10-190 U/L). Serum vitamin D₃ levels were 155 ng/mL (normal=30-80 ng/mL). Serum creatinine was 1.87 mg/dL (men=0.7-1.5 mg/dL, women=0.6-1.1 mg/dL), urea was 34 mg/dL (normal=10-40 mg/dL), serum uric acid concentration was 5.3 mg/dL (men=3.8-8.2 mg/dL, women=2.8-6.1 mg/dL), and serum calcium was 15 mg/dL (men=8.5-10.5 mg/dL, women=8.2-10.4 mg/dL). Her serum parathyroid hormone level was 3.95 pg/mL (normal=17-73 pg/mL). Liver function tests were well within the normal range. Chest radiograph and ultrasound of whole abdomen and pelvis were also normal.

Intervention and management

She was started on intravenous fluids, intramuscular calcitonin 240 IU thrice daily and oral furosemide 40 mg twice daily for hypercalcemia, after which she started showing rapid clinical improvement. On her follow-up for next 10 days, she was monitored for serum calcium levels on regular basis as they optimized to baseline levels within a couple of weeks. She was prescribed with an anti-diabetic along with the counseling on calcium-restricted diet at the time of discharge; she is doing well.

Discussion

Based on clinical history, examination, and lab investigations, a diagnosis of iatrogenic hypervitaminosis D was made. Iatrogenic hypervitaminosis D presents with typical symptoms of hypervitaminosis D, which includes nausea, anorexia, vomiting, hypercalcemia, etc. The cause includes high doses of intramuscular injections of vitamin D at frequent intervals or oral vitamin D supplementation for a long period, as was the case in our patient.^{2,4}

Current studies postulate a diagnostic cut-off of serum 25(OH)D level for hypervitaminosis D of more than 150 ng/mL or 325 nmol/mL.⁵ In spite of the significant reliance on serum calcidiol concentration for the evaluation and diagnosis of one's vitamin D status, toxicity of vitamin D can occur even at much lower serum calcidiol concentrations than the currently standardized concentrations of vitamin D toxicity.³

According to Gupta et al,⁵ diagnosis of symptomatic hypervitaminosis D can be made by the following criteria: (1) clinical features of hypercalcemia, (2) elevated serum calcium levels, (3) reduced or normal levels of serum parathyroid hormone (PTH), and (4) vitamin D levels of >100 ng/mL. However,

Institute of Medicine (IOM) committee presented an updated guideline on recommended daily intake of vitamin D and calcium. According to these guidelines, patients with serum 25(OH)D levels of >50 ng/mL are at risk of toxicity.⁶ Our patient fulfilled all the presented criteria of vitamin D toxicity.

According to Jensterle et al, vitamin D intoxication can be managed by discontinuing calcidiol, increasing salt and fluid intake, or additional hydration with intravenous saline; whereas severe cases can be managed more aggressively with intravenous hydration, diuretics, and glucocorticoids.⁷ In our case, we have managed the patient same way.

In this part of the world, vitamin D deficiency is very common, most notably among women due to inadequate sunlight exposure and dietary insufficiency. The daily dietary intake as recommended by US National Academy of Science is 15 µg/d (600 IU daily) recommended for the population of less than 70 years of age, and for individuals more than 70 years, 20 µg daily (800 units/d) is recommended. Methods such as sun exposure, fortified, and enriched foods are helpful in correction of mild vitamin D deficiency. Food and Nutritional Board, USA, has set a safe tolerable upper intake level (upper limit [UL]) of 50 µg (2000 IU) for vitamin D₃ due to the synthesis of 1,25(OH)₂D₃ being tightly regulated, extremely large doses of vitamin D, such as 100 000 units per day, are required to cause hypercalcemia.⁸

However, timely estimation of patients with the help of 24 hours urinary calcium excretion is necessary, the levels of which should not surpass 250 mg/d.³ It is a common practice for medical practitioners to prescribe vitamin D preparations for non-specific body ache, back ache, and leg pain that are partly believed to be as a result of deficiency state. However, self medication with more than the counter vitamin D preparations is also not uncommon. In most of the instances, multiple dosages of the commercially available preparation of 600 000 units are administered, which has the potential to result in vitamin D toxicity.⁹

A similar study was conducted in India in 2012, which reported a series of 15 cases of persistent vomiting due to iatrogenic hypervitaminosis D.¹⁰ To the best of our knowledge, we are reporting a first case of persistent vomiting as a result of vitamin D toxicity from Pakistan.

Vitamin D deficiency is one of the most important health concerns in our population, which is mostly treated overtly by giving large doses of vitamin D without monitoring, as was the case in our patient. It is, therefore, suggested that screening should be done at proper intervals to prevent vitamin D toxicities from occurring. Due to the lack of knowledge, financial resources, and proper laboratory setups among general population, regular screening for hypervitaminosis D or vitamin D deficiency is not applicable in our locality. Measures on the national level should be taken to establish better facilities for education and screening of common health-related issues. Strict policies and laws should be enforced against non-licensed practitioners to prevent such cases from happening.

Conclusions

Our case highlights the need for a pragmatic, but safe, approach while using empirical vitamin D supplements to avoid the rare scenario of serious adverse outcomes. It is strongly recommended that, all patients who present with vague non-specific symptoms like anorexia, vomiting, and fatigue, hypercalcemia due to hypervitaminosis D should be considered alongside the other usual causes. Awareness about the non-qualified mal-practitioners should be raised in general population, who prescribe more than the counter medications without adequate clinical knowledge.

Author Contributions

MIG contributed to principle idea, data collection, and critical revision of final work; SBB contributed to conception of work, manuscript writing, and literature search; AR contributed to manuscript writing and literature search; and AK contributed to data collection and literature search

Availability of Data and Material

All relevant articles discussed in our manuscript are available on Google Scholar and PubMed Central.

Consent for Publication

Both written and informed consent were taken from patient at the time of admission.

Ethical Approval

Our study is approved by the Institutional Review Board of Jinnah Medical College Hospital.

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