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CASE REPORT

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Vitamin D Toxicity Due to Self-Medication During the COVID-19 Pandemic – a Case Report

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ABSTRACT

Introduction: During the COVID-19 pandemic, vitamin D was used along with vitamin C and zinc as a preventive and curative therapy against SARS-CoV-2 infection. Vitamin D toxicity, even if it is rare, occurs when serum concentrations exceed 150 ng/mL and is usually manifested by hypercalcemia phenomena. **Case report:** We hereby report a case of two twin sisters who self-medicated with vitamin D in a dose of 4 × 4,000 IU/day for almost 10 months as a method of 'protection' against COVID-19, influenced by mass media advertising. The patients presented to the emergency department with hypervitaminosis D-related symptoms such as hypertension, headache, nausea, vomiting, and diffuse abdominal pain. Laboratory investigations revealed high levels of vitamin D and calcium. **Conclusions:** Vitamin D toxicity can lead to difficulties in positive and differential diagnosis because of the multiple complications of hypercalcemia.

Keywords: vitamin D toxicity, hypercalcemia, SARS-CoV-2, self-medication

INTRODUCTION

Vitamin D is an important secosteroid hormone that plays a significant role in maintaining the normal balance of calcium and phosphorus (Figure 1).[1,2] In addition to its important role in calcium metabolism, vitamin D is known for its immunomodulatory effects, as it can modulate innate and adaptive responses.[3] During the COVID-19 pandemic, vitamin D was used along with vitamin C and zinc as preventive and curative therapy against SARS-CoV-2 infection.[4] Vitamin D deficiency is a worldwide public health problem and is defined as a level of less than 20 ng/mL (Table 1).[5] Vitamin D toxicity occurs when serum concentrations exceed 150 ng/mL and is usually manifested in the form of hypercalcemia phenomena (Table 2).[6]

We hereby report a case of hypercalcemia due to vitamin D overdose as a method of 'protection' against SARS-CoV-2 infection.

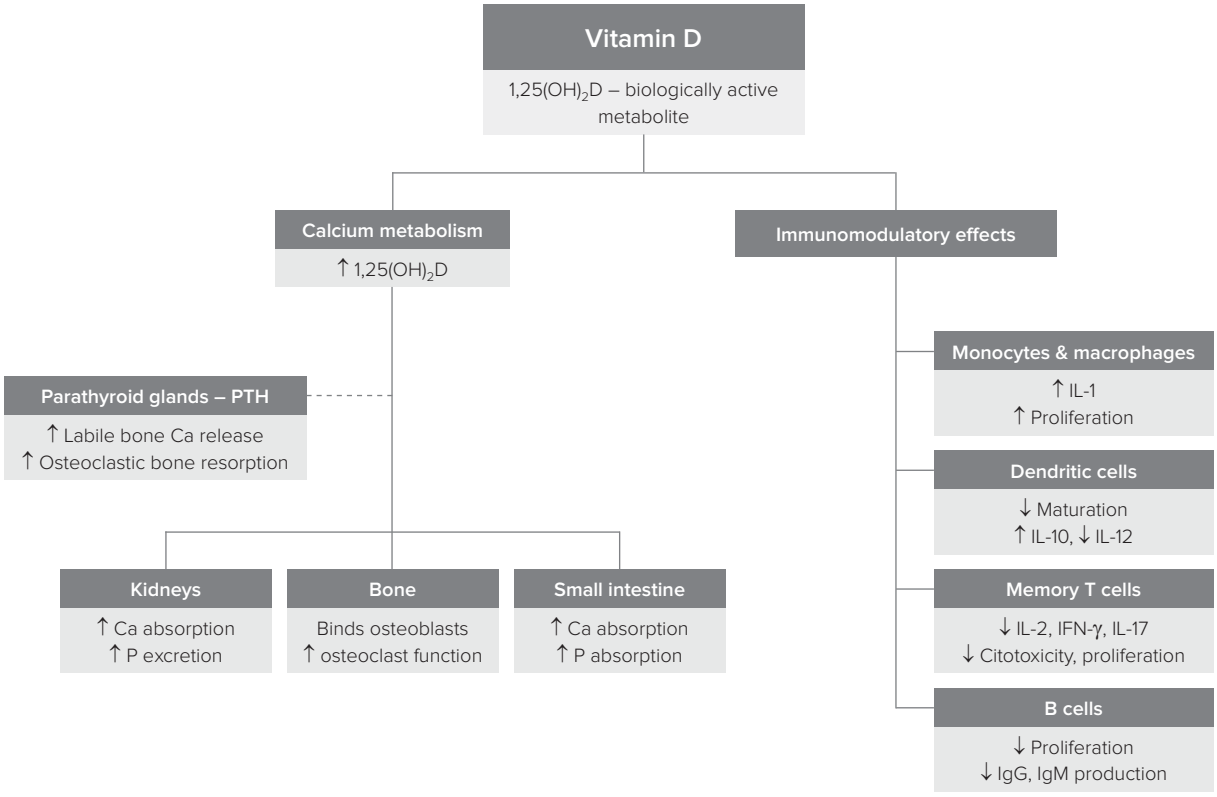


FIGURE 1. The role of vitamin D in calcium metabolism and its immunomodulatory effects[1,2]

Ca, calcium; P, phosphorus; IL-1, interleukin 1; IL-2, interleukin 2; IL-10, interleukin 10; IL-12, interleukin 12; IL-17, interleukin 17; IFN-γ, interferon gamma

CASE REPORT

In June 2022, two 27-year-old twin sisters with a history of borderline behavior disorder presented to the emergency department and were subsequently admitted to the Department of Internal Medicine for nausea, vomiting, headache, toothache, diffuse abdominal pain, constipation, fatigue, and hypertension over the past 3 weeks. The patients reported self-medication with vitamin D in a dose of 4 × 4,000 IU/day for almost 10 months as a method of 'protection' against COVID-19, influenced by mass media advertising.

TABLE 1. Diagnostic cut-off points for vitamin D concentrations[5]

Category	nmol/L	µg/L
Deficiency	<50	<20
Insufficiency	51–74	21–29
Sufficient	>75	>30
Excess	>250	>100
Intoxication	>375	>150

Laboratory investigations were performed in both patients. In one of them, they revealed the following pathological values: hemoglobin 11.6 g/L, creatinine 2.4 mg/dL, uric acid 12.7 mg/dL, vitamin D >150 µg/L, calcium 3.98 mmol/L, urine examination with 75 leukocytes/µL,

TABLE 2. Diagnostic cut-off points for vitamin D concentrations[5]

Category	Symptoms
Generalized	Fatigue Irritability
Gastrointestinal	Anorexia Constipation Nausea and vomiting
Musculoskeletal	Muscle weakness
Renal	Kidney stones Renal insufficiency
Central nervous system	Irritability Confusion Slurred speech Unstable gait
Metabolic	Dehydration Hypercalcemia

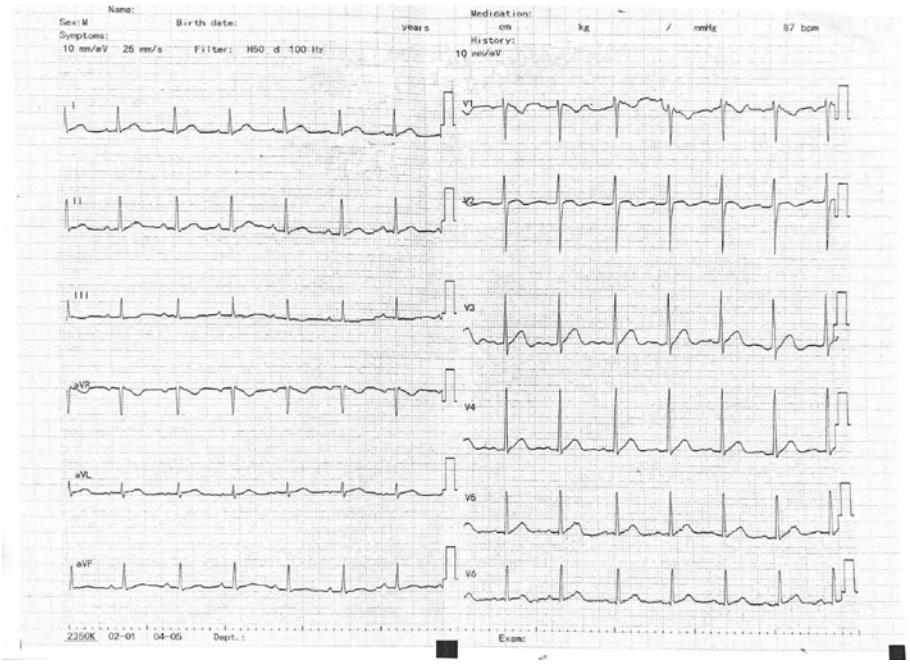


FIGURE 2. ECG of the first patient

negative nitrites. Laboratory examination of the other patient revealed the following pathological values: hemoglobin 11.5 g/L, creatinine 1.83 mg/dL, uric acid 11.3 mg/dL, vitamin D >150 μg/L, calcium 4.43 mmol/L, urine examination with 500 leukocytes/μL, negative nitrites. In both cases, the electrocardiograms (ECGs) showed ST-segment shortening (Figures 2 and 3). One day after admission, the laboratory tests were repeated and revealed a lower hemoglobin level – 9.7 g/L and 9.3 g/L – with no signs of bleeding. Gastroscopy was suggested, but the patients refused it. Parathyroid hormone or phosphorus levels were not determined in either case. Bacterial urine culture was negative in both cases. Ultrasonography of the abdomen showed decreased renal parenchymal index



FIGURE 3. ECG of the second patient

and poor corticomedullary differentiation of the kidney in both cases.

During admission to the Department of Internal Medicine, the patients were treated with intravenous saline, diuretics, and oral antihypertensive therapy, with regular monitoring of hemogram, renal function, vitamin D, and calcium levels. Creatinine and uric acid showed normalized values after 11 days.

The patients were discharged after 12 days with a prescription for low-calcium diet and antihypertensive therapy, and were advised to maintain good fluid intake. They were also advised not to take vitamin D and not to expose themselves to the sun.

In November 2022, the patients presented for a follow-up. Vitamin D was still high in both cases (510 ng/mL and 490 ng/mL). The patients agreed to the publication of their clinical data and this case report.

DISCUSSION

In December 2019, the outbreak of SARS-CoV-2 began in Wuhan, China, and rapidly spread worldwide, resulting in a global health crisis with significant psychological and socioeconomic consequences.[4] Because it is a highly virulent virus that is primarily spread through contact and respiratory droplets, people had to make radical choices to protect themselves such as isolation, wearing face masks, social distancing in public, and using preventive medicine.[2] During the pandemic, as well as today, the mass media heavily advertised vitamin and mineral supplements. Out of general concern, people tend to overdose on these supplements without consulting a physician.

Vitamin D is a fat-soluble vitamin that plays an important role in calcium metabolism, as well as in innate and adaptive immunity.[3] Vitamin D receptors are known to be expressed on T cells, B cells, and antigen-presenting cells. Vitamin D modulates immune function through its action on dendritic cells and T cells, which are involved in reducing the inflammatory response and promoting viral defense.[7] In addition, vitamin D plays a variety of roles, including regulating the transcription of antimicrobial peptides in different cell lines, contributing to the differentiation of monocytes and macrophages, and suppressing the production of proinflammatory cytokines.[8] Tang *et al.* demonstrated that normal vitamin D levels are associated with lower levels of IL-1 and IL-6.[9] The pathophysiology of SARS-CoV-2 infection includes the overproduction of several proinflammatory cytokines such as IL-1, TNF, IL-6, IL-12, IL-17, GM-CSF, and IFN-γ, which may trigger the cytokine storm.[2,8] Furthermore, vitamin D receptors have been identified in epithelial cells of the human respiratory tract, having the ability to regulate local respiratory homeostasis by upregulating the expression of antimicrobial peptides or by influencing viral replication.[8] Akbar *et al.* performed a meta-analysis with 14 studies and 999,179 participants, which showed that low serum vitamin D levels were associated with higher rates of SARS-CoV-2 infection, severe courses, and mortality.[10]

According to Amos *et al.*, vitamin D is involved in zinc homeostasis, which plays an important role in reducing coronavirus replication.[11] During the pandemic, and even today, vitamin D, vitamin C, and zinc are used as preventive medicine and are considered 'immunity boosters' by the general population.[4] Because of the general concern and perhaps because of the intense advertising in the mass media, people started self-medication with vitamins without considering the toxicity risk. As in our case, patients overdosed on vitamin D under the influence of media advertising. Also, the fact that they did not need a doctor's prescription encouraged them to self-medicate without consulting a physician. On the other hand, prescription errors can also lead to vitamin D toxicity, often being seen in patients requiring high doses for the treatment of various conditions.

Hypercalcemia is defined as a total calcium level greater than 2.5 mmol/L and is considered a medical emergency when it exceeds 3.5 mmol/L.[12] It has many manifestations including neurologic, cardiac, renal, and gastrointestinal.[12,13] The etiology of hypercalcemia includes malignancy, hyperparathyroidism, or osteoporosis, but in rare cases, it may be due to excessive vitamin D intake.[1,2,13,14] In our case, hypercalcemia occurred due to excessive vitamin D intake over a long period of time (16,000 IU/day for almost 10 months). The main complications in our case were hypertension and acute kidney injury. Being a fat-soluble vitamin, vitamin D is excreted slowly, which is why both patients had high serum vitamin D levels at follow-up.

CONCLUSION

Vitamin D toxicity, although rare, can lead to difficulties in positive and differential diagnosis because of the multiple complications of hypercalcemia. One of the factors contributing to vitamin D overdose is probably the intense advertising in the media and the possibility of obtaining the vitamin without a doctor's prescription.

As outlined, vitamin D is involved in immunity in many ways and plays an important role in the prevention and cure of SARS-CoV-2 infections by lowering the rate of infection, improving the course, and reducing mortality.

CONFLICT OF INTEREST

Parts of the case have been reported at the 2023 National Congress of the Romanian Society of Internal Medicine.

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