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Life-threatening hypercalcemia in a child with vitamin D intoxication due to parental self-medication: A case report

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Abstract

Vitamin D is essential for bone metabolism and has gained popularity since the general population is now more aware of its benefits. Unfortunately, the availability of unregulated vitamin D formulations without prescription increases the risk of inadvertently ingesting excessive doses of vitamin D. Reports of pediatric cases of vitamin D toxicity are scarce in the world literature. We present the case of a 4-years 9-months old boy from a rural town with vitamin D intoxication secondary to ingestion of seven oral vials containing each of them 600,000 Units of cholecalciferol for a period of 8 months. It is important to educate general population about the risks of ingesting vitamin D without medical prescription. In our patient, the most effective treatment strategy was the use of pamidronate.

Keywords

Vitamin D, pamidronate, child, hypercalcemia

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Introduction

Vitamin D is a fat-soluble vitamin essential for the absorption of calcium and phosphorus, as well as for bone and tooth metabolism.[1] Vitamin D has gained popularity since the medical community and the general population are now more aware of its benefits.[2] Unfortunately, the availability of unregulated vitamin D formulations without prescription increases the risk of inadvertently ingesting excessive doses of vitamin D[2,3] or self-medicating a child with toxic doses of vitamin D given by family members.[4–6]

Reports of pediatric cases of vitamin D toxicity are scarce in the world literature.[1,3,6–8] Especially in South America, it is hard to find reports of this type. Thus, we present the first report of a Peruvian child with vitamin D intoxication due to vitamin D supplement parental self-medication.

Case

A 4-years 9-months-old boy was admitted to our hospital because of vomiting (3–4 times per day), hyporexia, general malaise, high creatinine (1.27 mg/dL), and urea (74 mg/dL) levels, and an ultrasound showing bilateral parenchymal inflammatory nephropathy during the previous month. The ultrasound did not exhibit other findings. In the last 6 months, the patient also presented knee pain and weight loss (4 kg). On admission, the patient had the following physical exam findings: weight 17.5 kg (−0.22 SD), height 111.7 cm (+0.88 SD), body mass index (BMI) 14.0 (−1.49 SD), blood pressure 150/92 mmHg, and Tanner stage 1. Electrocardiogram findings included a sinus rhythm and short PR and corrected QT intervals. Blood tests showed: white blood cell count 9950, Hb 9.8 g/dL, platelet count 262,000, sodium (Na) 131 mEq/L, potassium (K) 2.68 mEq/L, calcium (Ca) 19.6 mg/dL (4.89 mmol/L), phosphorus (P) 4.7 mg/dL, creatinine

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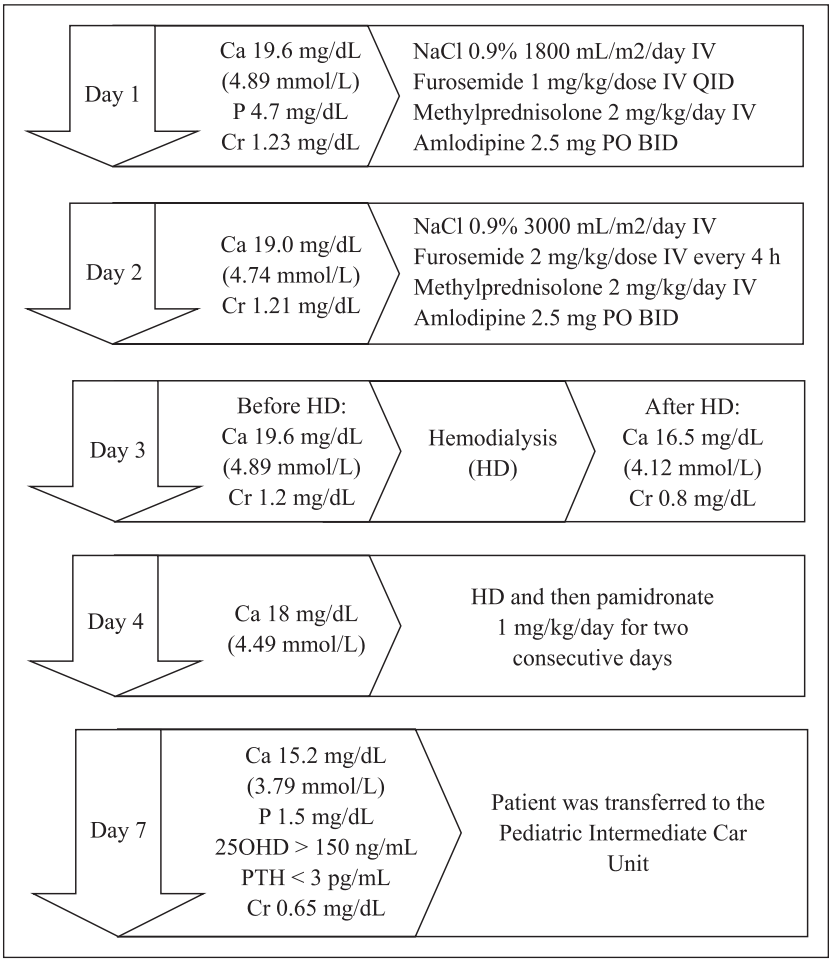

Figure 1. Evolution of the patient in the Pediatric Intensive Care Unit.

1.23 mg/dL, C-reactive protein 2.6 mg/dL, lactate dehydrogenase 187 U/L, alkaline phosphatase 118 U/L, and normal liver and coagulation profiles. With these results, the patient was quickly transferred to the Pediatric Intensive Care Unit (PICU) on the same day.

On the first day in the PICU, the patient received the following treatment: 0.9% NaCl 1800 mL/m^2/day IV, furosemide 1 mg/kg/dose intravenous (IV) QID (four times a day), methylprednisolone 2 mg/kg/day IV, and amlodipine 2.5 mg PO BID (two times a day). The parents said that during the last 8 months, they self-administered to the child seven oral vials containing 600,000 Units of cholecalciferol because they thought vitamin D was harmless. The following day, laboratory results showed: Ca 19.0 (4.74 mmol/L) and Cr 1.21 mg/dL. Thus, the intravenous hydration rate was increased to 3000 mL/m^2/day, and the furosemide dose was increased to 2 mg/kg/dose IV QID. On the 3rd day, Ca and creatinine serum levels were 19.6 (4.89 mmol/L) and 1.2 mg/dL, respectively. The patient was submitted to hemodialysis, after which Ca and creatinine levels decreased to 16.5 (4.12 mmol/L) and 0.8 mg/dL, respectively. However, the next day Ca levels rose to 18 mg/dL (4.49 mmol/L). Thus, hemodialysis was repeated and then 1 mg/kg/day IV pamidronate was administered for 2 consecutive days. On the 7th day, laboratory studies showed: Ca 15.2 mg/dL (3.79 mmol/L), P 1.5 mg/dL, 25-hydroxyvitamin D (25OHD) >150 ng/mL, parathyroid hormone (PTH) <3 pg/mL, and creatinine 0.65 mg/dL. Thus, the patient was transferred to the Pediatric Intermediate Care Unit (PINCU) on the same day. The evolution of the patient in the PICU is represented graphically in Figure 1.

On admission to the PINCU, the electrocardiogram was normal. Methylprednisolone was discontinued, and prednisone was started at 25 mg/day. Intravenous hydration was reduced to 2480 mL/m^2/day, and the dose of furosemide to 15 mg IV every 8 h. Methyldopa was started at 125 mg PO every 8 h due to the persistence of arterial hypertension despite the use of amlodipine. Because of the low serum P level found on admission to PINCU (1.5 mg/dL), potassium phosphate 3 mmol/L IV was administered, after which the P level increased to 2.0 mg/dL. The patient also received a 150 mL packed red blood cell transfusion due to an Hb level of 7 g/dL, after which it increased to 11 g/dL. One week later, the patient was transferred to the Pediatric Specialties Hospitalization Ward (PSHW).

On the day the patient was admitted to the PSHW, serum Ca and P levels were 12.2 (3.04 mmol/L) and 2.0 mg/dL,

Table 1. Laboratory results in chronological order.

Laboratory tests	Day 1	Day 2	Day 3 (pre HD)	Day 3 (post HD)	Day 4	Day 7	Day 8	Day 15	Day 16	Day 22	Reference values
Ca (mg/dL)	19.6	19	19.6	16.5	18	15.2		12.2		8.5	9.2–10.5
Ca (mmol/L)	4.89	4.74	4.89	4.12	4.49	3.79		3.04		2.12	2.3–2.62
P (mg/dL)	4.7					1.5	2.0	2.0	1.6	5.0	4.3–6.8
Mg (mg/dL)										1.64	2.09–2.84
25OHD (ng/mL)						>150					20–100
PTH (pg/mL)						<3					9–74
ALP (U/L)	118										111–277
Cr (mg/dL)	1.23	1.21	1.2	0.8		0.65					0.20–0.43
Na (mEq/L)	131										132–141
K (mEq/L)	2.68										3.3–4.7
LDH (U/L)	187										192–321
CRP (mg/dL)	2.6										<1.41
Hb (g/dL)	9.8					7.0	11.0				11.4–14.3
WBC (×1000/μL)	9.95										4.4–12.9
PLT (×1000/μL)	262										187.4–444.6

ALP, alkaline phosphatase; Ca, calcium (total); Cr, creatinine; CRP, C-reactive protein; Hb, hemoglobin; HD, hemodialysis; K, potassium; LDH, lactate dehydrogenase; Mg, magnesium; Na, sodium; 25OHD, 25-hydroxyvitamin D; P, phosphorus; PLT, platelet count; PTH, parathyroid hormone; WBC, white blood cell count.

respectively. On the 2nd day, serum P level decreased to 1.6 mg/dL and Joulie's solution (1 mmol/L of phosphate) PO 13 mL every 8 h was started. Between the 3rd and the 7th day, clinical and laboratory abnormalities subsided. Therefore, all medication was progressively withdrawn. On the 8th day, the patient presented serum Ca, P, and Mg levels of 8.5 (2.12 mmol/L), 5.0, and 1.64 mg/dL, respectively. The patient was discharged the next day. All laboratory results in chronological order can be found in Table 1.

The patient was last seen after discharge when he was 6 years and 2 months old, completely asymptomatic, and with normal growth: weight 20.3 kg (−0.31 SD), height 121.2 cm (+0.87 SD), and BMI 13.8 (−1.56 SD).

Discussion

Vitamin D toxicity is often associated with high-dose supplement intake.[1] Some supplements exist as unlicensed formulations,[1] which sometimes erroneously have excessive vitamin D concentrations.[9,10] There is also a lack of education about vitamin D toxicity in the general community.[1,5] This paucity of information among parents leads to an important risk of parental self-medication in children. Our patient is an example of this.

Vitamin D toxicity is defined as hypercalcemia and 25OHD >250 nmol/L (100 ng/mL) with hypercalciuria and suppressed PTH.[11] The upper limit of daily oral vitamin D for healthy children aged <1 and 1–3 years are reported as 1000–1500 and 2000–2500 IU, respectively.[12] Hypervitaminosis D leads to hypercalcemia because vitamin D excess overwhelms the capacity of 24-hydroxylase (vitamin D catabolic enzyme), which increases the amount of a vitamin D metabolite reaching the vitamin D receptor (VDR) in the nucleus of target cells.[13] This metabolite probably is 25OHD,[3,13] and its activating effect over the VDR stimulates calcium absorption in the intestine.[1] Previously, the excess of 1α,25-dihydroxyvitamin D (1,25(OH)D) was also hypothesized as a potential responsible for vitamin D toxicity.[13,14] However, it seems it is not the main toxic metabolite that leads to hypercalcemia.[13] Our patient had a 25OHD value >150 ng/mL and suppressed PTH, which is suggestive of vitamin D toxicity according to the definition provided above, even in the absence of urinary calcium measurements since the clinical and biochemical characteristics upon admission, as well as response to treatment, were consistent with vitamin D toxicity.

Vitamin D intoxication can result in gastrointestinal (loss of appetite, vomiting, and constipation), renal (polyuria, hypercalciuria, and nephrocalcinosis), central nervous system (headache), cardiovascular (shortened QT interval, elevated ST segment, bradyarrhythmia, first-degree heart block, vascular calcifications, and hypertension), musculoskeletal (bone and joint pain), and ophthalmological and skin complications.[1,4,6,12] Pediatric cases have been associated with renal failure requiring hemodialysis and death attributed to acute pancreatitis.[5] Our patient had gastrointestinal and cardiovascular signs of toxicity, as well as joint pain and renal failure requiring hemodialysis. However, hemodialysis was not efficient in lowering calcium levels.

Management of vitamin D-dependent hypercalcemia mainly involves vitamin D supplement withdrawal, low calcium diet, IV vigorous rehydration, loop diuretics, glucocorticoids, and bisphosphonates.[13]

Mild hypercalcemia (<12 mg/dL (<2.99 mmol/L))[15] only requires calcium and vitamin D dietary restriction and an increase in oral water intake.[16] However, moderate (12 to

<14 mg/dL (2.99 to <3.49 mmol/L))[15] and severe (⩾14 mg/dL (⩾3.49 mmol/L))[15] hypercalcemia require hospitalization.[16]

In the inpatient setting, Kara et al.[16] suggest hydration with a fluid load of 10–20 mL/kg/h with 0.9% saline and a maintenance fluid at a rate of 1.2–2 times the usual daily requirement, furosemide 1–2 mg/kg/day IV q8–12 h, and then a pamidronate infusion of 1 mg/kg over 4 h in moderate cases and 2 mg/kg over 8 h in severe hypercalcemia, and repeating the same dose if hypercalcemia persists >14 mg/dL (>3.49 mmol/L) on day 5 or >12 mg/dL (>2.99 mmol/L) on day 7.

Bisphosphonates can lower calcium levels via their antiresorptive effect on bones.[12] Several studies reveal that pamidronate is effective and safe in children for the treatment of hypercalcemia secondary to vitamin D intoxication and malignancy.[8] There are fewer publications about using zoledronic acid in children.[4,8] However, they suggest that zoledronic acid could be superior to pamidronate.[8] The potential advantages of zoledronic acid compared to pamidronate include a faster effect, lack of need for several repeated doses, and shorter hospitalization time.[8] In our patient, we used pamidronate instead of zoledronic acid because, in our setting, there has been more experience using pamidronate for the treatment of severe hypercalcemia.

Side effects include fever and abnormal renal function.[17] Our patient did not have symptoms suggestive of adverse effects. However, hypophosphatemia was likely secondary to the rapid decrease in serum calcium levels since there is a case report in which this relatively rapid decline after pamidronate therapy induced hypophosphatemia secondary to hyperparathyroidism.[17]

Loop diuretics inhibit calcium reabsorption in the thick ascending limb of Henle.[13] Glucocorticoids decrease renal and intestinal absorption of calcium[12] and inhibit the conversion of serum 25(OH)D3 into active 1,25(OH)2D3.[13] However, they seem less effective than other regimens.[12]

A limitation of our report is that we did not find ionized calcium measurements in the clinical record. However, high total serum calcium levels, the previous excessive ingestion of vitamin D, and the clinical picture of the patient before and after admission are consistent with a classic case of severe hypercalcemia. Besides, the amount of vitamin D ingested before and the very high levels of 25OHD were the best reasonable explanation for the clinical picture. Another limitation is the lack of urinary calcium measurements. However, we know that the patient had an ultrasound without nephrocalcinosis at admission.

Conclusion

In conclusion, it is important to educate the general population about the risks of ingesting vitamin D without a medical prescription. Education must reach especially parents to prevent vitamin D toxicity in children. In our patient, the most effective treatment was the use of pamidronate.

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None.

Author contributions

M.A.V.-L. and G.A.-G. conceptualized and designed this case report; M.A.V.-L. and R.I.Z.-S. collected the data about the patient. All authors analyzed and interpreted the information recorded. M.A.V.-L. and H.F.F.-N. reviewed the literature; M.A.V.-L. and G.A.-G. wrote the manuscript. All authors provided a critical review of the final manuscript.

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Ethics approval

Ethical approval to report this case was obtained from Hospital Nacional Edgardo Rebagliati Martins Institutional Review Board (AUT. No. 063-CE-GHNERM-GRPR-ESSALUD-2024).

Informed consent

Written informed consent was obtained from the mother of the patient for his anonymized information to be published in this case report.

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