Residência RP Pediátrica
Publicação Oficial da Sociedade Brasileira de Pediatria
ISSN-Online: 2236-6814

Submitted on: 09/23/2021
Approved on: 07/03/2023

CASE REPORT

# SEVERE HYPERCALCEMIA INDUCED BY IATROGENIC HYPERVITAMINOSIS D: CASE REPORT

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**Keywords:**
Hypercalcemia, Vitamin D, Case Reports, Infant.

## Abstract

**INTRODUCTION:** Vitamin D intoxication among nurslings (serum levels of 25-hydroxyvitamin D above 150 ng/mL) is a factor in the development of hypercalcemia, an uncommon condition in pediatrics. **OBJECTIVE:** Report a case of severe hypercalcemia caused by hypervitaminosis D in a nursling. **CASE REPORT:** 5-months-old masculine child, exclusively breastfed, referred to a specialist with suspected cows milk protein allergy because he failed to gain weight in the last month and presented with blood and mucus in stool. Beyond failure to thrive, the patient evolved with somnolence, apathy and hypotonia. Laboratorial tests revealed hypercalcemia (serum calcium of 17,40 mg/dL) and hypervitaminosis D (180 ng/mL). The hypothesis of vitamin D intoxication was raised and later confirmed by the laboratorial analysis of the supplement offered to the nursling, which revealed a vitamin D concentration 46 times greater than the originally prescribed by the pediatrician. **CONCLUSION:** Due to the currently high diagnostic suspicion of cows milk protein allergy in nurslings, other causes of these symptoms cant be neglected in the investigation when the elimination diet fails. In this nursling, the persistence of failure to thrive, apathy, anorexia and hypotonia during four months motivated the investigation that showed a severe hypercalcemia due to the usage of manipulated vitamin D.

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Resid Pediatr. 2023;13(4).
DOI: 10.25060/residpediatr-2023.v13n4-736

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## INTRODUCTION

Vitamin D consists of a prohormone (secosteroid) that acts on the absorption of calcium and phosphorus by the intestine, on the reabsorption of calcium by the kidneys and on the mineralization of bones.[1] Vitamin D intoxication in infants, considered for serum levels of 25-hydroxyvitamin D higher than 100 ng/mL, according to the Clinical Practice Guidelines of the Endocrinology Society, is one of the causes for the development of hypercalcemia (serum calcium levels greater than 10.5mg/dL), an uncommon condition in pediatrics.[2] Clinical conditions involving vitamin D intoxication are rarely reported, since hypercalcemia suggests other diagnostic hypotheses, such as primary hyperparathyroidism, neoplasms, infections and use of thiazide diuretics.[3]

The objective of this report is to describe a pediatric case of severe hypercalcemia due to hypervitaminosis D in an infant, leading to loss of weight and height gain (failure to thrive) and hypotonia.

## CASE REPORT

Male infant, 5 months old, born at term measuring 49.5cm, born in Curitiba-PR, exclusively breastfed until this age, presented to the outpatient clinic of the specialist pediatrician of the Nutritional Care Program – Curitiba (PAN-Curitiba) , due to suspected cow's milk protein allergy (CMPA). PAN-Curitiba is the program that provides high-cost formulas for infants in Curitiba with special food needs. In this consultation, weight was 6,600g (< Z score -1), height 62.3cm (Z score -2 to -1), weight/height ratio in Z score -1 to 0 (weight and height measurements in graphs 1 and 2). The symptoms that generated the hypothesis of CMPA were the absence of weight gain during the previous month and the presence of streaks of mucus and blood in the feces, with the first episode occurring sporadically at three months and twenty days of age, after a respiratory infection, but it has been repeated every day for the last 25 days (after the 4 month vaccinations).

For the next two months, he remained breastfed, with his mother's diet being without cow's milk and dairy products, with the introduction of complementary foods at the right age. The presence of blood in the feces lasted a total of 45 days and disappeared after adjusting the diet. At 7 months, weight and height had both fallen to the Z -3 to -2 score (height gain was only 3.5 cm in the previous four months – a drop of two channels on the height chart; weight was maintained in 6,600g for four months). In addition to FTT, he developed drowsiness, apathy, anorexia and hypotonia, which were progressively worse. The mother, after two months of a strict exclusion diet for her and her son, was impatient with the diagnosis of CMPA given by the pediatricians, as she did not see any improvement in the symptoms, which were even getting worse.

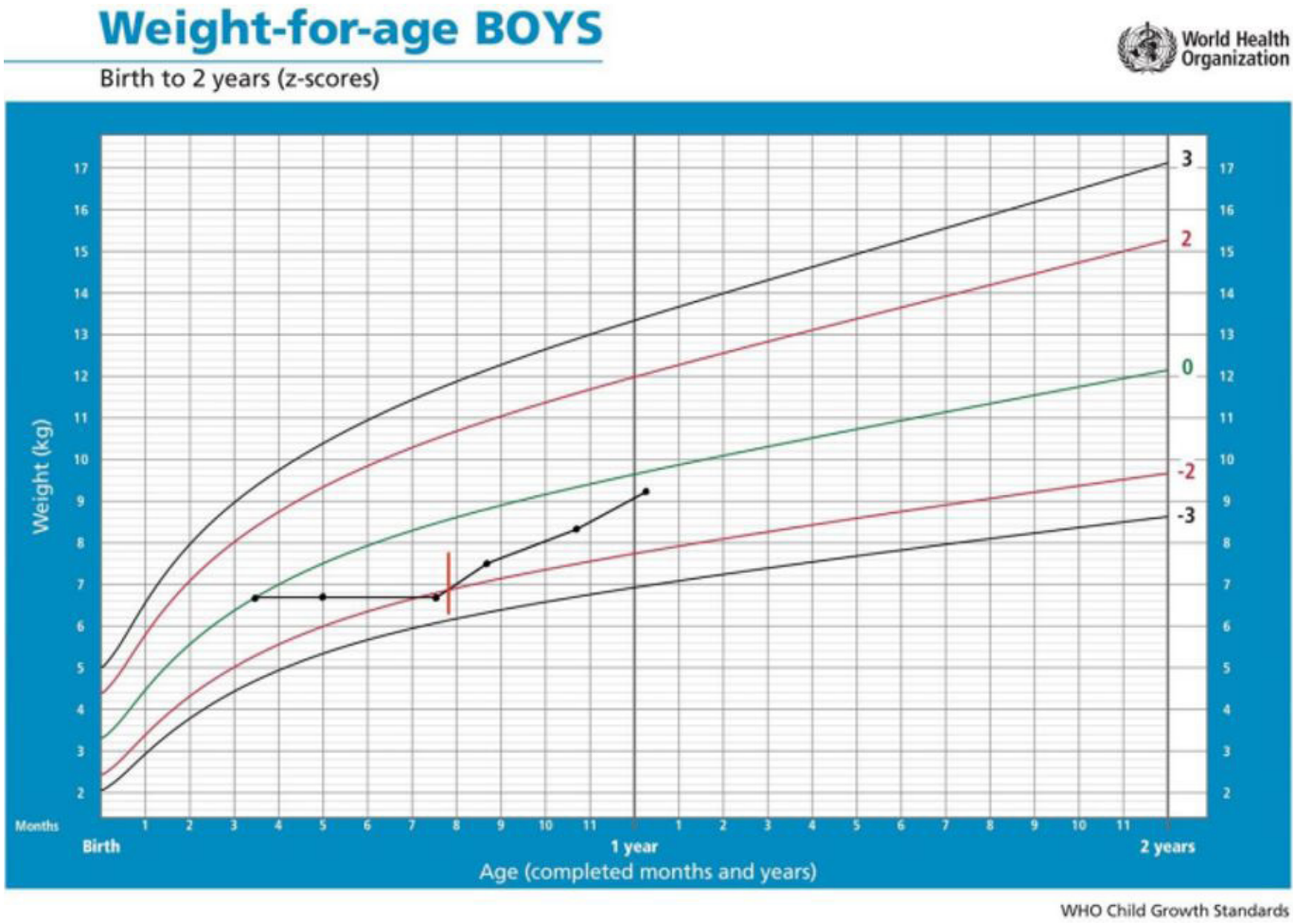
He was 7 months and 22 days old and was sent to the Pediatric Emergency to perform additional hematological, metabolic, biochemical, serological and urinalysis tests. The calcium level of 17.40 mg/dL led to immediate hospital admission for treatment and investigation of the cause of hypercalcemia. He was admitted to the Intensive Care Unit (ICU), where he received hydration and the use of diuretics to reduce his serum calcium level. During the investigation, he showed hypervitaminosis D (vitamin D = 180 ng/ml). He was discharged after seven days, when serum calcium levels reached 12.7 mg/dL and serum vitamin D levels reached 90 ng/mL. We considered the hypothesis of vitamin D intoxication. He had been receiving oral vitamin D drops since the second month of life. The pharmacological preparation of the vitamin supplement had been carried out in a compounding pharmacy, under the guidance of the pediatrician, with a prescribed concentration of 10,000 IU/ml. The bottle produced by the pharmacist was sent for laboratory analysis of vitamin D concentration, and a concentration of 465,878 IU/ml of this vitamin was detected, approximately 46 times higher than the medical prescription.

After one month of stopping the use of the supplement, at 9 months, the patient was in rapid nutritional recovery, very active and with normal muscle tone. He continued breastfeeding, consuming other food stuffs appropriate for his age and received an extensively hydrolyzed protein formula after 8 months. At 12 months, an oral challenge test with cow's milk protein was performed, without any adverse reaction. Weight was in the z-1 to 0 score and height was in the z-2 to -1 score. He had normal values for calcium, vitamin D, parathyroid hormone, urea and creatinine. The phosphorus concentration was still above the reference and he continued being followed by the endocrinology department.

## DISCUSSION

Clinical pediatricians have currently acted with a high level of diagnostic suspicion of CMPA in infants, given a variety of symptoms. The case presented here serves as a warning for pediatricians not to neglect the differential diagnosis and the search for other causes, especially when the protein exclusion diet fails. In the patient described, the cause of FTT, apathy, anorexia and hypotonia was investigated, resulting in the surprising finding of hypercalcemia due to hypervitaminosis D. The resolution of signs and symptoms was complete in the following months after removal of the manipulated supplement, with a drop in levels of circulating calcium and vitamin D.

Symptoms associated with hypercalcemia in children may be nonspecific. Some of the clinical findings related to hypercalcemia may include failure to gain weight and height, lethargy, hypotonia, polyuria, nephrolithiasis, vomiting, bone pain, abdominal pain, constipation and rarely convulsions.[4] Marked elevation of calcium can be treated with 20mL/ kg

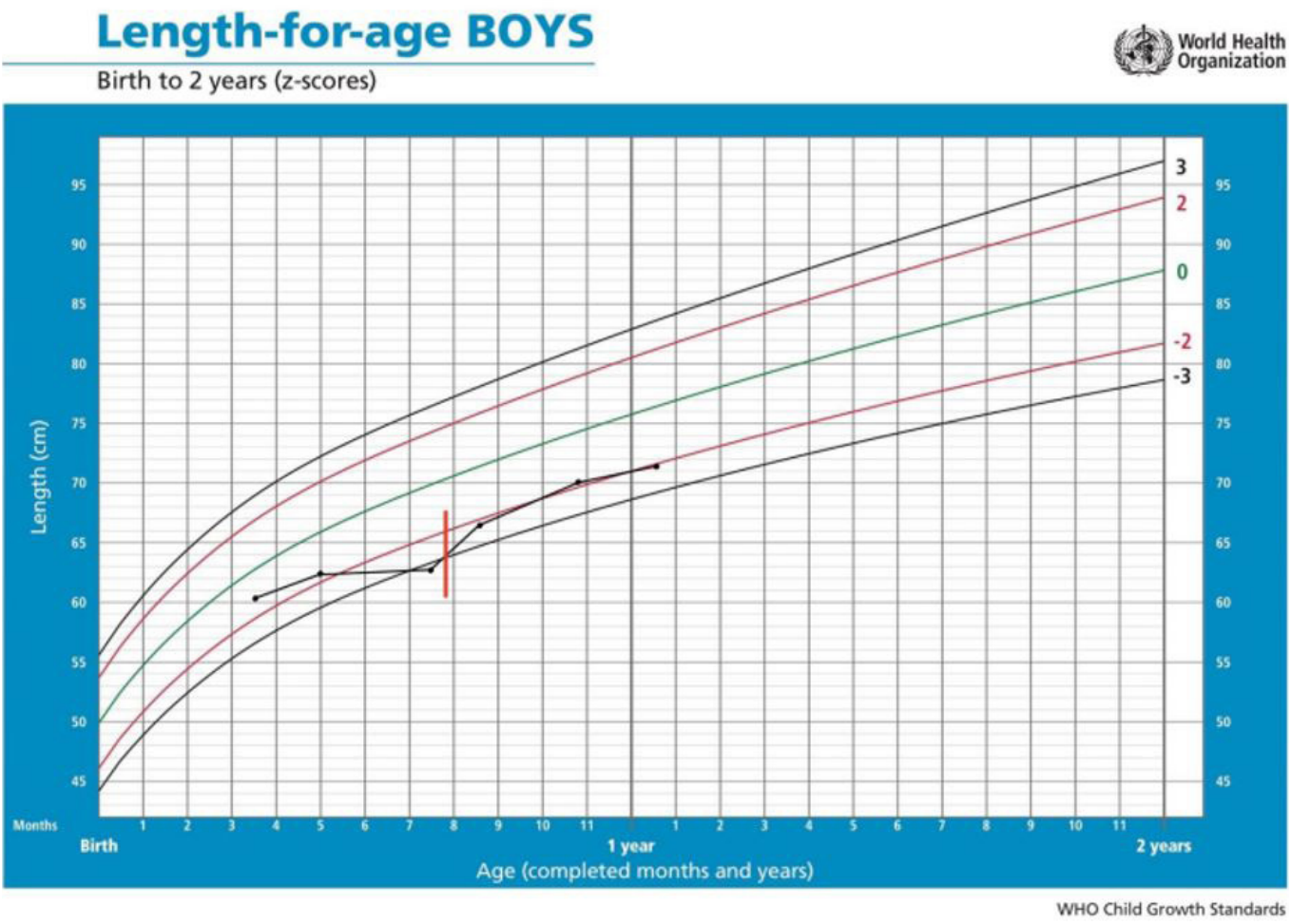



**Graph 1.** Weight by age
**Legend:** The red line represents the moment when the administration of the vitamin D supplement was interrupted.

of IV saline added with 2 mg/kg of IV furosemide. In cases of persistent severe hypercalcemia, corticosteroids, calcitonin or bisphosphonates can be added to the treatment.[5] In addition to kidney disease, in chronic and severe cases of hypercalcemia, whether or not caused by hypervitaminosis D, cardiovascular evaluation is necessary. A case of an 11-year-old child with chronic kidney disease and secondary hyperparathyroidism was described, which progressed to ischemic cerebral necrosis, calcification in the coronary arteries and myocardial infarction, due to calcium deposition in the patient's vascular system.[6]

Maternal vitamin D deficiency is a risk factor for vitamin D deficiency in childhood, as infants depend on breast milk, which has a low vitamin D content (around 20-60 IU/L), sometimes being insufficient to the child's nutritional needs.[7] Therefore, the Department of Endocrinology of the Brazilian Society of Pediatrics recommends prophylactic supplementation of 400 IU/day from the first week of life until 12 months, and 600 IU/day from 12 to 24 months, including children on exclusive breastfeeding. For preterm newborns, supplementation with 400 IU/day of vitamin D should be started when their weight exceeds 1500g and when there is full tolerance to enteral nutrition. Supplementation aims to prevent hypovitaminosis D and, consequently, rickets, hypocalcemia, hypophosphatemia, tetany, skull tabes and osteomalacia.[8] Other studies also associate hypovitaminosis D with higher incidences of acute lower respiratory tract infections and recurrent wheezing in the first five years of life.[7]

Occasionally, the commercial supply of pharmaceutical products intended for vitamin D supplementation in infants becomes scarce. This situation encourages an increase in the prescription of compounded supplements, which increases the risk of vitamin poisoning.[8] The product from compounding pharmacies must have its composition carefully monitored.




**Graph 2 - Height by age.**
**Legend:** The red line represents the moment when the administration of the vitamin D supplement was interrupted.

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