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Case Report

Vitamin D Intoxication in Children: A Case Report

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Abstract: Vitamin D is a crucial hormone in phosphocalcium homeostasis. Although vitamin D intoxication is rare, its complications can be dramatic, affecting both the short-term vital prognosis and long-term renal function. We report here a case of hypercalcemia due to vitamin D intoxication, with the aim of analyzing the factors that contribute to vitamin D intoxication, assessing the consequences of this intoxication on the child's health, and proposing recommendations for appropriate management. The patient was a 6-year-old child with a history of common nutritional rickets for which he had been receiving vitamin D supplementation. The patient was admitted to the pediatric emergency department of Children's Hospital in Rabat for incoercible vomiting and acute dehydration. Biological assessment showed severe hypercalcemia at 150mg/l, hypercalciuria at 192 mg /24 hours. The serum level of 25(OH) vitamin D was greater than 154 ng/ml. The diagnosis retained was as hypercalcemia due to vitamin D intoxication, confirmed by an in-depth interview with the parents, who found a over administration of the recommended dose. The evolution was marked by chronic kidney disease due to nephrocalcinosis (creatinine clearance according to the SCHWARTZ formula 17 ml/min). Heterogeneity of the expression forms of vitamin D dosages and intake regimens leads to confusion and increases the risk of misuse, as in the case of our patient, where a misreading of the medical prescription led to the intentional ingestion of toxic doses, hence the need for close and adequate medical supervision and awareness of vitamin D supplement use among healthcare professionals and parents.

Keywords: Vitamin D, Intoxication, Children, Chronic kidney Disease.

INTRODUCTION

Vitamin D is a crucial hormone in phosphocalcium homeostasis. Although vitamin D intoxication is rare, its complications can be dramatic, affecting both the short-term vital prognosis and long-term renal function. Vitamin D intoxication remains a problem in developing countries. In Morocco, it is mostly iatrogenic.

We report here a case of major hypercalcemia due to vitamin D intoxication following a dosing error, in a child monitored for common nutritional rickets.

The aim of this work is to analyze the factors that contribute to vitamin D intoxication, assess the consequences of this intoxication on the child's health, and propose recommendations for appropriate management; emphasizing the importance of preventing such situations by educating parents and healthcare professionals on good practices in terms of supplementation and medical follow-up.

OBSERVATION

We report a case of a 6-year-old child with a history of common nutritional rickets since the age of 1 month, for which he had been receiving vitamin D supplementation.

The patient was admitted to the pediatric emergency department of the Children's Hospital in Rabat for incoercible vomiting, asthenia and anorexia. On admission, the child was confused and drowsy, apyretic, hemodynamically and respiratorily stable; the clinical examination revealed hypotrophy with dehydration estimated at 10%. The abdominal examination was normal.

Biological assessment showed severe hypercalcemia at 150mg/l (84-102) with a normal total protein level of 71 g/l (64-83), hyperphosphatemia at 60 mg /l (23-47), hopoparathyroidism intact PTH< 4 pg/ml (6.5-38. 8), urea at 0.50 g/l (0.15-0.46) and creatinine at 16 mg/l (7.2-12.5), The calciuria was elevated at 192 mg

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/24 hours with a calciuria/creatinuria ratio of 1.06. The serum level of 25(OH) vitamin D was greater than 154 ng/ml (375 nmol/L) (9.4 - 52.4). The results of the remaining assessment were normal.

The diagnosis retained was hypercalcemia due to vitamin D intoxication, confirmed by an in-depth interview with the parents, who found a mistake in the posology of vitamin D treatment; the patient was in fact receiving one ampoule of Sterogyl® 15 (600,000 units per 1.5 ml) per day, and this lasted two months instead of taking the prescribed Sterogyl® drops.

The child was hospitalized in the pediatric unit for management of hypercalcemia consisting of hyperhydration, administration of intravenous furosemide and prednisone 5 mg daily per os, two infusions of pamidronate and interruption of taking native vitamin D.

In order to evaluate the impact of this intoxication, an electrocardiogram (ECG) was performed, showing no abnormalities. Renal ultrasound revealed hyperechoic lesions of the Malpighian pyramids suggestive of a bilateral nephrocalcinosis.

The evolution was marked by gradual correction of objective hydration and calcium levels, but with persistent chronic kidney disease (creatinine at 18 mg/l and creatinine clearance according to the SCHWARTZ formula 17 ml/min), with an ultrasound appearance in favor of chronic renal insufficiency: slightly diminished kidneys of moderately differentiated size) (Figures 1 and 2).

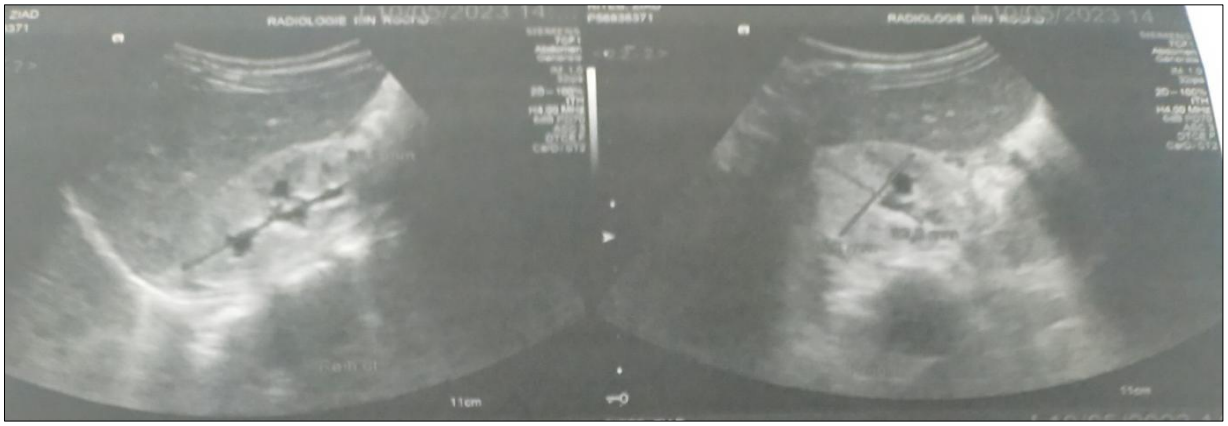

Figure 1: Right renal ultrasound showing an appearance in favor of chronic kidney disease: the right kidney is slightly reduced in size with regular contours and echogenic cortex, moderately differentiated measuring= 60 × 32 × 35 mm.

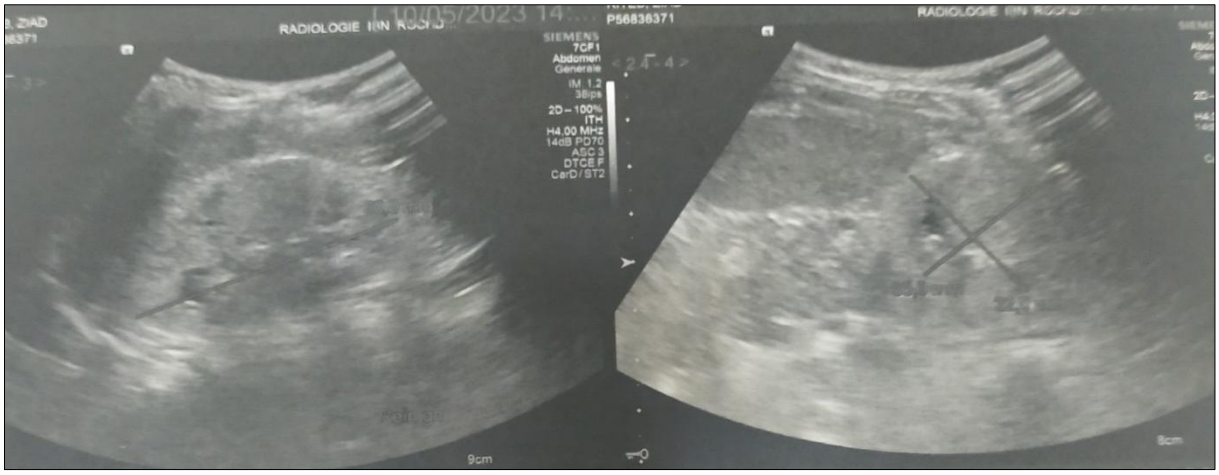

Figure 2: Left renal ultrasound ultrasonography showing an appearance in favor of chronic kidney disease: the left kidney is slightly reduced in size with regular contours and an echogenic cortex, moderately differentiated, measuring 60 × 30 × 32 mm

DISCUSSION

Vitamin D is a major component of phosphocalcium homeostasis through its active metabolite, 1,25 (OH) 2 D. Its absence can lead to bone demineralization leads to nutritional rickets in children. Therefore, the treatment of this chronic disease consists of administering vitamin D; However, this therapeutic approach may expose the patient to the risk of vitamin D intoxication due to repetitive prescriptions of high doses, self-medication by parents seeking to enhance their child's growth, prescription errors [1], or in rare cases by misreading of medical prescription by the pharmacist, as seen in our patient's case.

Today, vitamin D is recognized as a vitamin with multiple potentialities, as it is involved in numerous physiological processes. Due to its dual dietary and endogenous origins, vitamin D is a vitamin in a class of its own, and should be considered a pre-pro-hormone. Vitamin D metabolism is well understood and involves two hydroxylation processes. First, is hepatic hydroxylation that leads to form 25-hydroxy vitamin D (25(OH)D). Second is renal hydroxylation leading produce 1,25-dihydroxy vitamin D (1,25(OH)2D) or calcitriol, the active vitamin D metabolite. This metabolite is responsible for the various genomic and non-genomic effects of vitamin D, whose mechanisms of action involves a specific nuclear receptor, the vitamin D receptor (VDR), and various signaling pathways controlled by a membrane receptor, the protein disulfide isomerase family A member 3 (Pdia3) [2, 3].

Since hydroxylation of vitamin D on carbon 25 in the liver is not subject to any regulation; serum 25(OH)D concentration is a good reflection of endogenous and exogenous vitamin intake, and constitutes the best biological parameter for defining vitamin D status [4]. Vitamin D intoxication refers to serum 25(OH) D levels, particularly when the level exceeds 100 ng/mL (250 nmol/L) [5]. In the context of patient supplementation, there are two forms of vitamin D available on the market: vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol) [6]. It is therefore important to mention that assay kits are capable of measuring both forms of vitamin D (25OHD3 and 25OHD2), to avoid minimizing and to prevent underestimating the results of individual assays supplemented with one form or the other of vitamin D [7, 8].

Currently, two methods are employed to assess 25OH Vit D: immunological methods and separative non-immunological, direct-detection methods. Immunological methods include competitive assays in which 25(OH) Vit D and a labeled tracer compete for recognition by an anti-25(OH) Vit D antibody. These markers may be isotopes, enzymes, or phosphorescent molecules in radioimmunoassay, enzyme immunoassay, or luminoimmunoassay methods. On the other hand, non-immunological methods rely on the physical separation of molecules using high-performance liquid chromatography or mass spectrometry. While the laters are more accurate, they are also more expensive and are usually reserved for specialized or research laboratories. Whichever assay method is adopted, 25OH Vit D must be completely dissociated from the carrier proteins before it can be accurately quantified [9].

Furthermore, there is currently no standardized assay method in Morocco, which makes it difficult to establish reference values, and reduces comparability between results. We therefore recommend carrying out controls in the same laboratory, or in a laboratory using an identical assay technique [9].

Vitamin D intake increases the concentration of vitamin D itself and of many other vitamin D metabolites, especially 25(OH)D. In hypervitaminosis D, the concentrations of vitamin D metabolites, such as vitamin D, 25(OH) D, 24,25(OH)2D, 25,26(OH)2D, and 25(OH)D-26,23- lactone, increase significantly (22). Abnormally increased concentrations of vitamin D metabolites exceed the VDBP (Vitamin D Binding Protein). Binding capacity and cause a release of free 1, 25(OH) 2D; the latter active metabolite enters the target cells by diffusion and acts through the VDR (Vitamin D receptor) [10].

Excess vitamin D is stored in fatty tissues, since it is fat-soluble. Toxic effects may therefore persist for more than 2 months after exogenous intakes have been discontinued [11, 12].

The clinical manifestations of vitamin D toxicity may vary but they are mainly related to hypercalcemia. They may be similar to those of other hypercalcemic states and include neuropsychiatric disorders such as difficulty concentrating, confusion, somnolence, depression and in extreme cases stupor and coma, gastrointestinal symptoms such as recurrent vomiting, abdominal pain, polydipsia, anorexia, constipation, gastric ulcers and pancreatitis. Cardiovascular complications include hypertension, shortened QT interval, ST-segment elevation and bradyarrhythmias with first-degree heart block on the electrocardiogram, as well as renal symptoms such as hypercalciuria as the first sign, polyuria, polydipsia, dehydration, nephrocalcinosis and renal failure [10, 13].

Recent clinical cases have highlighted the seriousness of vitamin D intoxication, with the risk of nephrocalcinosis and rhythm disorders secondary to hypercalcemia; indeed, doses in excess of 50,000 IU/day increase the concentration of 25-OH-vitamin D to over 150 ng/mL (or 374 nmol/L), and are associated with hypercalcemia and hyperphosphatemia [14]. The threshold for potential vitamin D toxicity has been shown to be lower, at around 4,000 IU/day with chronic administration. More recently, it has been shown that the administration of high doses of periodic loading, 600,000 IU every 4 to 6 months, is likely to lead to hypercalcemia, hypercalciuria and may cause sequelae such as nephrocalcinosis or kidney stones [15-17].

In pediatrics, there is no consensus. When the serum concentration of 25-OH-vitamin D exceeds 200 nmol/L, the toxic effects of vitamin D can be observed, especially hypercalcemia and hyperphosphatemia [14].

Heterogeneity of expression forms of vitamin D dosages and intake regimens lead to confusion and increase the risk of misuse, as in the case of our patient, where a misreading of the medical prescription concerning the form of vitamin D prescribed led to the intentional ingestion of high toxic doses.

In our situation, several factors can contribute to vitamin D intoxication:

- The Lack of regular, careful monitoring of treatment through biological assays of vitamin D, calcium levels and calciuria
- The deficiency in the explanations provided by the prescribing physician to the parents regarding the therapeutic protocol for vitamin D supplementation
- The level of illiteracy among parents and their lack of awareness regarding the importance of properly following medical instructions and monitoring doses administered
- The illegibility of the medical prescription, which could be the cause of the error
- The lack of communication between the doctor and the pharmacist.

The treatment involves discontinuation of all vitamin D intake, and a low-calcium diet until calciuria and blood calcium levels are completely normalized. Intravenous rehydration and diuretics are the first line of treatment for moderate hypercalcemia. Glucocorticoids and calcitonin have been used in severe cases to lower elevated calcium concentrations. However, the effect of glucocorticoids is slow, and calcitonin is intolerable for some patients due to the risk of hypersensitivity. In addition, both products have side effects. More recently, biphosphonates, inhibitors of bone resorption, represent an effective alternative in the treatment of vitamin D intoxication. Intravenous pamidronate and oral alendronate are the most widely used, and they both have shown rapid efficiency in correcting calcium levels and calciuria [1-18].

Preventing this type of intoxication is likely the best way to avoid potentially serious and fatal complications. To achieve this, recommendations can be made for healthcare professionals [1-4]:

It is recommended that doctors:

- Clearly and appropriately explain to parents the method of administering the treatment using simple language, while ensuring that they have fully understood the therapeutic protocol,
- to Ensure that recommended doses are respected at the next check-up,
- to Avoid changing marketed dosage forms, especially for patients with chronic conditions such as rickets,
- Be vigilant when prescribing these vitamin supplements, ensuring that prescriptions are perfectly legible, especially in our Moroccan context where prescriptions are often handwritten, or better still provide computerized prescriptions to avoid the problems associated with handwriting and guarantee clear communication with pharmacists,
- Regular monitoring of the treatment of vitamin D deficiency and rickets by measuring blood vitamin D levels in the same laboratory and using the same technique, mentioning that the patient is on supplementation, to enable the medical biologist to interpret the vitamin D results correctly [19],
- Do not prescribe sterogyl® 600,000 IU ampoules for the maintenance treatment of rickets, due to their high vitamin D content.

Similarly, it is essential that parents are aware of the dangers of over-consumption of vitamin D in children, and follow medical recommendations on dosage and frequency of administration [1-4].

Pharmacists must also play a crucial role in advising patients on the appropriate use of vitamin D supplements, and in checking the doses prescribed by doctors. Effective communication between all those involved in healthcare is therefore essential to prevent such serious incidents and to ensure effective treatment and patient safety.

Finally, vitamin D supplementation must adhere precise rules: neither too much, nor too little. The SFP 2012 recommendations should be respected, but not exceeded [4-14].

CONCLUSION

Cases of vitamin D intoxication, although less frequent, still occur, and their consequences can be severe. This case serves as a reminder of the need for close and adequate medical supervision and awareness of vitamin D supplement use among healthcare professionals and parents. It is crucial to rase awareness among healthcare providers about the risks associated with vitamin D misuse to prevent such intoxication and to detect it as early as possible. In conclusion, preventing vitamin D intoxication requires a cautious approach and heightened awareness of its potential dangers.

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