Hypervitaminosis D causing nephrogenic diabetes insipidus in a 5-month-old infant

Ihab A. Ahmad, MBBS, MD, *Abdulmoein E. Al-Agha,* DCH, FRCPCH.

ABSTRACT

يعزي العواقب الوخيمة للتسمم الناتج عن زيادة نسبة فيتامين د في مرحلة الطفولة إلى فرط كلس الدم الحاد وينتج عنه تكلس الكلي ولقد لوحظ أن العلاجات الحالية للتسمم الناتج عن زيادة فيتامين د بالدم غير مقنعة وتؤدي إلى فرط كلس الدم لفترات طويلة . نستعرض هنا حالة طفل عمره خمسة أشهر يعاني من عدم القدرة علي النمو ورفض الطعام وتأخر التطور ونقص توتر جذعي، والجفاف . وكانت الأسمولية له بالبلازما ونسبة الصوديوم بالدم عالية بشكل ملحوظ، في حين الأسمولية له بالبول كان منخفضاً بشكل غير لائق ولم تستجب للعلاج بعقار ديزموبريسين في الوريد . تم تشخيص حالته بمرض السكري الكلوي الكاذب بسبب فرط كالسيوم الدم الناجم عن زيادة نسبة فيتامين د بالدم وتم علاجه بالماء وعقار هيدروكلوروثيازيد .

Vitamin D intoxication in infancy leads to acute hypercalcemia and subsequent hypercalcuria with nephrocalcinosis. Strategies used for patients with vitamin D intoxication are unsatisfactory and associated with prolonged periods of hypercalcemia. We present a 5-month-old infant who had failure to thrive, refusal to feed, delayed motor development, truncal hypotonia, and dehydration. She had high plasma sodium and osmolality with low urine osmolality, and did not respond to intravenous desmopressin administration. She was diagnosed as nephrogenic diabetes insipidus due to hypercalcemia caused by hypervitaminosis D, and was treated with hydrochlorothiazide 2 mg/kg twice daily, and hydration.

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From the Pediatrics Department, King Abdulaziz University Hospital, Jeddah, Kingdom of Saudi Arabia.

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Address correspondence and reprint request to: Dr. Ihab A. Ahmad, Pediatrics Department, King Abdulaziz University Hospital, PO Box 80215, Jeddah 21589, Kingdom of Saudi Arabia. Tel. +966 502464675. E-mail: captennemo2002@hotmail.com

Vitamin D intoxication (VDI) usually results from prescribing high doses of vitamin D by health care providers. Meanwhile, patients may wrongly ingest high doses. Parents sometimes give high doses of vitamin D to infants and children complaining from delayed teething, delayed walking, and knock-knee.[1] There is no consensus yet regarding the dose of vitamin D, which may lead to intoxication, but maintenance of vitamin D has been reported to be safe at 1000 IU/day for ages 0-1, 2500 IU/day for ages 1-3, 3000 IU/day for ages 3-8, and 4000 IU/day for age 9 and above, adults, and pregnant women.[2] Hypervitaminosis D occurs when the 25 hydroxy vitamin D (25-OH (D) level, the main storage form of vitamin D exceeds 150 ng/mL (20-80).[1] Patients may also experience nonspecific symptoms such as nausea, vomiting, anorexia, confusion, and weakness, typically secondary to the resulting hypercalcemia.[3] We present this case to shade lights on VDI as vitamin D usually taken without prescription, and physicians should regularly follow up vitamin D level for children receiving vitamin D.

Case Report. We present a 5-month-old female infant, a product of 30 weeks gestation with birth weight of 0.944 kg, had a history of hyaline membrane disease, for which she received one dose of Survanta. She was put on total parenteral nutrition for 4 weeks but did not receive diuretics. She started to develop polyuria (urine output >4.8 ml/kg/h), failure to gain weight, and persistent hypernatremia (156-165 mmol/L). Three months prior to her presentation, she was on full fortified formula feeding in addition to a total of 1400 international units (IU) of vitamin D (800 IU as maintenance plus extra 600 IU from multivitamin syrup) for prophylaxis of osteopenia of prematurity (serum

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calcium was 2.21 mmol/L, serum phosphorus was 1.02 mmol/L and alkaline phosphatase was 186 u/L before starting vitamin D). Her weight on presentation was 2.2 kg below the fifth percentile. All vital signs were normal. Other significant findings in the physical examination included a nondistended abdomen with normal active bowel sounds, and neurologic examination revealed truncal hypotonia and delayed motor development. Laboratory testing confirmed a diagnosis of diabetes insipidus (**Table 1**). Magnetic resonance of the brain and posterior pituitary was normal. She was given diagnostic intravenous desmopressin drip one mIU/kg/hr with no response clinically and biochemically, which established the diagnosis of nephrogenic diabetes insipidus (NDI). Regarding hypercalcemia, the investigations showed evidence of hypervitaminosis D (**Table 1**). Renal ultrasound confirmed the presence of medullary nephrocalcinosis (**Figure 1**). The patient was diagnosed as NDI caused by hypervitaminosis D. Management was planned by cessation of vitamin D, starting hydrochlorothiazide 2mg/kg/BID, low calcium milk formula, and hydration with 0.9 normal saline in order to avoid sudden drop on serum sodium then, shifted to 0.45 normal saline until serum sodium was normalized after 10 days. She showed marked improvement regarding clinical and biochemical features of NDI within 10 days duration, while there was much slower improvement in Vitamin D status up to 3 months duration with a drop to132 nmol/l.

Table 1 - Laboratory data of a 5-month-old infant with hypervitaminosis D presented in a study at the Pediatrics Department, King Abdulaziz University Hospital, Jeddah, Kingdom of Saudi Arabia.

Laboratory tests	Results	Normal value
Serum sodium	156 mmol/L	136-145
Serum potassium	4.5 mmol/L	3.5-5.1
Serum chloride	112 mmol/L	98-107
Blood urea nitrogen	12.9 mmol/L	2.5-6.4
Creatinine	103 mmol/L	53-115
Serum phosphorus	1.8 mmol/L	0.81-1.58
Glucose	5.6mmol/L	3.9-6.7
Serum magnesium	1.3 mmol/L	0.7-1.0
Serum calcium	2.95 mmol/L	2.15-2.5
Alkaline phosphatase	209 u/L	50-136
Albumin	26 g/L	34-50
Urine specific gravity	1000	1005-1025
Urine osmolality	20 mosmol/kg	500-800
Serum osmolality	320 mosmol/kg	282-295
25 hydroxy vitamin D	175 nmol/L	50-80
Parathormone hormone	0.7 pmol/L	1.6-6.9
Urine calcium	6.52 mmol/L	0.5-4.37
Urine sodium	10 mmol/L	41-115
Urine potassium	12.7 mmol/L	10-60
Urine chloride	10 mmol/L	15-40
pH	7.399	7.38-7.45
Bicarbonate	20.9 mmol/L	22-24.2

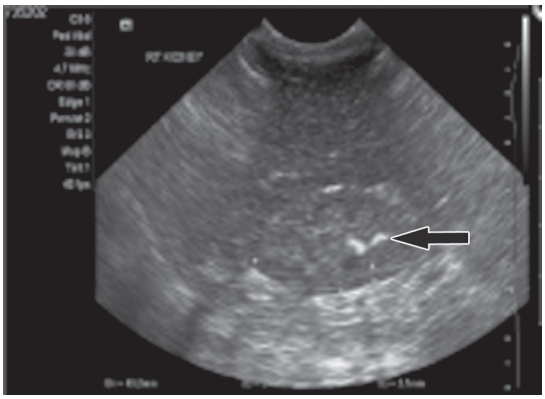

Figure 1 - A pelvic ultrasound of the patient showing medullary nephrocalcinosis (arrow).

Discussion. Hypervitaminosis D occurs if vitamin D is taken in excess and manifestation related to hypercalcemia, hypercalciuria, and metastatic calcification.[4] The NDI usually presents with polyuria, polydipsia, dehydration, fever, constipation, vomiting, failure to thrive, and developmental delay.[5] The characteristic laboratory findings of vitamin D intoxication are high serum calcium level, normal or high serum phosphate level, low parathormone, and high vitamin D levels.[6] Hypercalcemia resulting from vitamin D intoxication is always associated with hypercalciuria. Hypercalcemia leads to nephrocalcinosis by overloading the renal resorptive mechanism.[6] The main goal of treatment of VDI in children is the correction of hypercalcemia, which has to be carried out as an emergency, if the total calcium concentration is >3 mmol/l due to the adverse effects of hypercalcemia on cardiovascular, central nervous, renal, and gastrointestinal systems.[7] Treatment is designed to provide: sufficient water to maintain normal electrolytes; low renal solute load to minimize water loss; and adequate calories to support growth. Pharmacotherapy usually is needed. Thiazide diuretics are used along with modest salt restriction to reduce the delivery of filtrate to the diluting segments of the nephron. They exert their effect by decreasing sodium and chloride absorption in the distal tubule, thereby allowing more sodium absorption and therefore more water absorption in the proximal tubule.[8]

In our case, there was an association of NDI with hypervitaminosis D in comparison to reported cases

of iatrogenic vitamin D intoxication in infants were associated with hypercalcemia only without NDI and none of them developed hypernatremia like our case.[9]

The recommended vitamin D dose in premature infants is 400-800 IU.[10] In our patient, she received 1400 unit per day for 3 months before developing nephrocalcinosis and NDI. The half-life of vitamin D is 2 months due to storage in the adipose tissue, and it is 2 weeks in the circulation. Hypercalcemia lasts for more than 6 months following VDI.[6] Patients with VDI need follow-up until the 25-OH (D) and calcium return to normal levels as hypercalcemia might re-occur.

In conclusion, we would like to vigorously emphasize that if higher doses of vitamin D need to be used in preterm babies, serum vitamin D and calcium should be regularly monitored in order to avoid vitamin D intoxication.

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