Case Report

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An interesting case of unintentional vitamin D toxicity in an infant due to erroneous supplement concentration: a case report

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Introduction and importance: Despite the rare occurrence of vitamin D toxicity in infants, increased use of vitamin D formulations as well as incorrect supplement concentration by manufacturing pharmaceutical companies, has contributed to an increased incidence of vitamin D toxicity. Over-the-counter vitamin D preparation constitutes variable concentrations that can render life-threatening consequences in children.

Case presentation: Here, we present a case of a 2.5-month-old infant presenting with failure to thrive. The clinical presentations were nasal blockage, noisy breathing, poor feeding, lethargy, dehydration, and fever for 3 days with decreased appetite. Her urine culture report showed a urinary tract infection. The biochemical evaluation demonstrated raised total serum calcium (6.0 mmol/l) and serum 25-hydroxy vitamin D (> 160 ng/ml) with suppressed parathyroid hormone concentration (3.7 pg/ml), which was the major concern to the clinicians. On ultrasonographical examination, nephrocalcinosis was observed. Further evaluation unveiled that the vitamin D supplement administered to the infant constituted a deucedly high dose of 42 000 IU instead of the recommended dose of 0.5 ml of 800 IU.

Clinical discussion: The patient developed vitamin D toxicity after consuming a mega dose of vitamin D supplements due to a manufacturer error.

Conclusions: Hypervitaminosis D has severe life-threatening consequences like failure to thrive in otherwise healthy-born infants. Regular monitoring of vitamin D supplements administered in infants by medicinal practitioners and strict supervision of all stages of the production process by pharmaceutical companies is crucial to prevent complications from supplement overdose.

Keywords: case report, hypercalcemia, hypervitaminosis D, infant, nephrocalcinosis, vitamin D toxicity

Introduction

Mother's milk has a low concentration of vitamin D (20–60 IU/l) which could run out within 8 weeks if breastfed infants do not receive vitamin D supplements[1]. In recent years, the empirical prescription of supplemental vitamin D has been increasing rampantly due to the observed increase in cases of nutritional rickets in infants and children[2,3]. Along with the increase in the use of the supplements, cases of intoxication and overdose are also increasing, resulting in hypercalcemia and related complications[4]. The irrational use of vitamin D is an issue of concern even in our country, Nepal. Here, we present an unusual case of a 2.5-month-old healthy-born female infant with vitamin D toxicity due to a concentration error in the supplement following SCARE (Surgical CAse REport) guidelines[5].

HIGHLIGHTS

- Vitamin D toxicity is an uncommon finding in infants.
- Pragmatic use of supplemental vitamin D has been increasing due to nutritional rickets in infants and children.
- With an increasing trend in the use of supplements, cases of intoxication and overdose are in upsurge resulting in hypercalcemia and related complications.
- Vitamin D intoxication due to concentration errors in supplements in newborn infants or children is devastating and should always be determined early.

Case presentation

A 2.5-month female infant with no drug history, family history including any relevant genetic information, and psychosocial history was referred to the pediatric ward of our hospital when

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she visited the Pediatric Outpatient Department with the chief complaint of fever for 3 days, nasal blockage, and refusal to feed along with the diagnosis of failure to thrive. The fever was relieved with a paracetamol (Niko) drop. Before she was referred to our hospital, she was admitted to a tertiary care hospital elsewhere in the capital city with anuria for 12 h where the diagnosis of poor intake was made. The condition was corrected by administering intravenous (i.v.) fluid and discharged after counseling on feeding.

Following a few days of discharge, her guardian noticed a low-grade fever, nasal blockage, and difficulty feeding, for which she was admitted to our center. On the day of admission to the hospital, a physical examination revealed low-grade fever (37.8°C), a heart rate of 112 beats per min, a respiratory rate of 32 breaths per min, and a SpO_2 of 97%. The infant appeared sick and weak. Her systemic examination was not contributory. Though she was a healthy term infant weighing 3120 g at birth, her current weight, length, and head circumference, along with her *z*-score for the WHO chart for age, were 3400 g (< – 3 *z*-score), 56 cm (0 to – 2 *z*-score), and 36 cm (– 2 to – 3 *z*-score). Also, her weight-for-length *z*-score was < – 3.

Investigations

Her complete blood count was within normal range. Microbiological investigations were sent to establish the cause of the fever. Her urine examination showed a white cell count of 30–40 cells/high-power field and a trace amount of albumin. Later, she was diagnosed with a urinary tract infection with positive culture reports for *Escherichia coli*. She was then given injectable cefotaxime (Cefot) and amikacin (Mika-N). The liver function tests revealed aspartate aminotransferase of 130 U/l (normal range, 5–40), alanine transaminase of 120 U/l (normal range, 5–45), alkaline phosphatase of 248 U/l (normal range, <145). Her renal function test was within the normal range. Total calcium was elevated up to 6.0 mmol/l (normal range, 2.1–2.5), along with normal serum phosphorus of 6.3 mg/dl (normal range in children, 4.0–7.0).

Since the mother had a history of hypothyroidism and was under levothyroxine (Thyronorm), to rule out congenital thyroid disorder, a blood test of the infant was sent for a thyroid function test which was found to be within normal range.

Ultrasonography of the abdomen and pelvis showed bilateral medullary nephrocalcinosis, that is nephrocalcinosis in the left kidney and right kidney, respectively (Fig. 1A, B) with normal rest scan.

On further evaluation for the etiology of hypercalcemia, 25-hydroxy vitamin D (25-OHD) level and intact parathyroid hormone (iPTH) investigations were performed, which showed an elevated level of a 25-OHD of greater than 160 ng/ml (normal range, 30–50), and lower iPTH level of 3.7 pg/ml (normal range, 15–68.3). Spot urinary calcium was 0.86 mmol/l and the urinary calcium (Ca)–creatinine ratio was 0.2 (normal range, 0.1–0.3), ruling out hypercalciuria. Further investigation revealed that the infant received 0.5 ml of around 42 000 IU orally of vitamin D3 (Biodee) supplement having batch no. 621-750. However, 400 IU/ml of vitamin D3 is the prescribed dose for a healthy infant. These findings are suggestive of vitamin D intoxication with hypercalcemia, with the absence of evidence of hyperparathyroidism, acute kidney disease, chronic kidney disease, and multiple myeloma.

Treatment

She was treated with intravenous fluid and prednisolone (Omnacortil) for hypercalcemia, while the vitamin D supplement was discontinued. She was then discharged after 5 days on gradual improvement. Serum total calcium and 25-OHD levels decreased progressively to reach the normal range over the next 2 months when assessed in a follow-up visit. Also, there was weight gain, and the patient weighed around 6400 g at 4.5 months which was normal as per the WHO chart per age (0 to – 2 *z*-score). However, she still has issues regarding bilateral medullary nephrocalcinosis (Fig. 2A, B) along with the normal left lobe of the liver and foci of linear calcification within the right lobe of hepatic parenchyma (Fig. 3A, B) with no clinical signs.

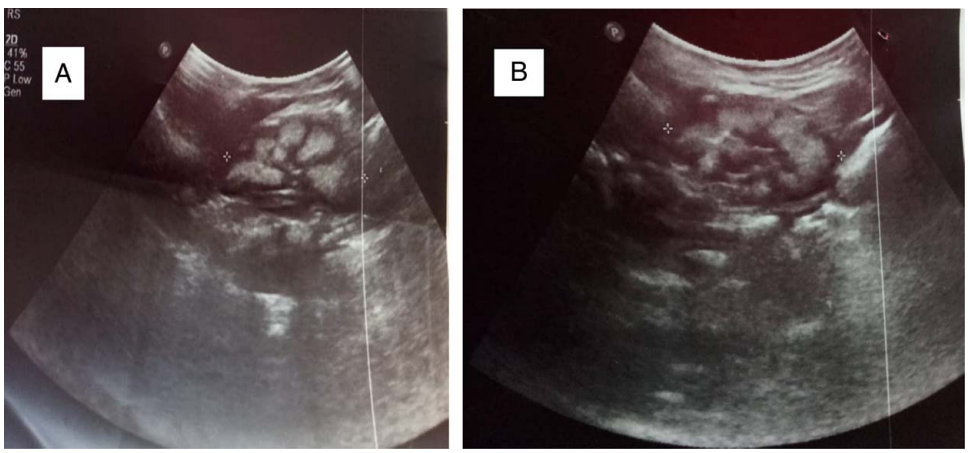

Figure 1. Bilateral kidneys with features suggestive of (F/S/O) medullary nephrocalcinosis. (A) Ultrasound scan showing left kidney with medullary nephrocalcinosis. (B) Ultrasound image of a right kidney showing medullary nephrocalcinosis.

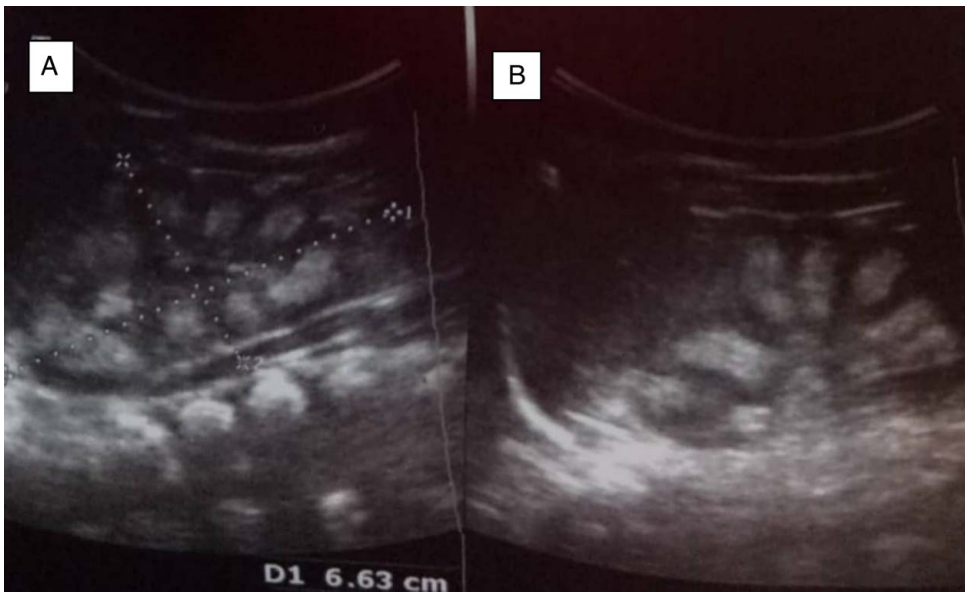

Figure 2. Enlarged bilateral medullary nephrocalcinosis on follow-up after 2 months. (A) An ultrasound scan of the left kidney showed medullary nephrocalcinosis. (B) Ultrasound scan of the right kidney showed medullary nephrocalcinosis.

Discussion

In this report, we have presented the life-threatening consequences faced by a healthy, term-born, 2.5-month-old girl after consuming a mega dose of vitamin D supplements due to manufacturer error. Constant daily intake of five times more than the recommended daily allowance (RDA) of vitamin D, that is 1800 IU in children and 4000 IU in adults, has been reported as toxic[6–8]. Our patient had taken 0.5 ml of 42 000 IU of vitamin D, an amount as high as 21 times the upper limit of the toxic dose, since the third day of birth. Therefore, the cause of hypercalcemia was established as high doses of vitamin D. This kind of manufacturer error could result in a devastating effect on human life. The pharmaceutical company seriously failed in our case and was notified as a preventive measure to avoid new events by discontinuing defective batches from the market.

Our case of hypervitaminosis D was similar to the case report documented by Marins *et al.*[9] due to manufacturer error; however, the case was presented in a 53-year-old male. Also, four cases of neonatal hypercalcemia have been reported in Rodd and Goodyer[10] that include cases like hypercalcemia in prematurely born babies due to calcium supplementation (iatrogenic), due to severe neonatal hyperparathyroidism, Williams syndrome, and due to parenteral nutrition postdelivery hypercalcemia in a patient born with a cleft lip and palate, respectively. However, hypercalcemia in healthy and term-born infants due to manufacturer error in vitamin D supplements, as seen in our case, has not been reported so far. Hence, this case report may add value

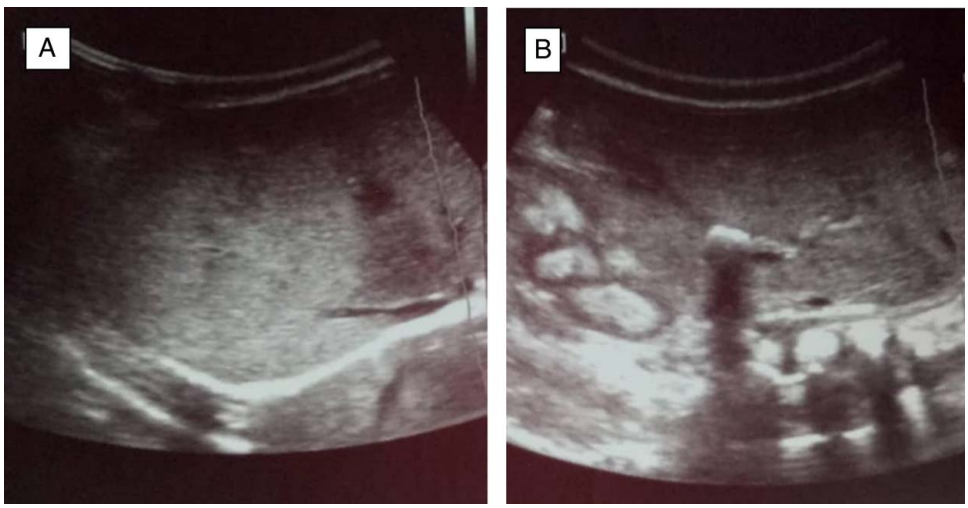

Figure 3. Ultrasonography (USG) images of the liver. (A) USG of the left lobe of the liver showed no calcification. (B) USG of the right lobe of hepatic parenchyma showed few foci of linear calcification.

and evidence of new cases to existing literature. Also, hypercalcemia may have led to nephrocalcinosis and urinary track infection due to the complication of excess vitamin D[11–13].

Conclusion

Vitamin D hypervitaminosis can lead to life-threatening conditions in infants, and therefore we suggest manufacturing pharmaceutical companies promote good practices, establish quality criteria and perform correct dilution, weighing, and conversion procedures. In addition, medical practitioners should prescribe authorized vitamin D and supervise vitamin D supplements in infants to intervene in complicated cases on time with signs of toxicity or overdose. This case report could be an alarm of alertness among the triad of a pharmacist, medicinal practitioners, and parents.

Ethical approval

This is a case report: therefore, it did not require ethical approval from the ethics committee.

Consent

Written informed consent was obtained from the patient for the publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contribution

All authors were involved in writing the paper, collecting data, revising it critically for important intellectual content, and reviewing and editing it.

Conflicts of interest disclosure

There are no conflicts of interest.

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