Chapter 2
Vitamin D Deficiency in Infants

Oranan Siwamogsatham and Vin Tangpricha

Case Presentation

A 6-month-old male Turkish infant presented with fever and three recent episodes of generalized seizures, each episode lasting for approximately 5 min. This patient was reported well until the day of admission when his skin felt warm followed by an episode of generalized seizures. He was born full term and was exclusively breastfed since birth, with no vitamin supplementation. Family history was negative for epilepsy. His parents were not
cosanguineous. His mother followed the Islamic faith and dressed with most of her skin covered. She did not take vitamin supplements during pregnancy or lactation. On examination, the infant was drowsy after the epileptic spell. The temperature was 38 °C, the blood pressure 90/45 mmHg, the pulse 140 beats per minute, and the respiratory rate 40 breaths per minute. His weight, height, and head circumference were in 97th percentile for age. There was no bulging of the anterior fontanelle. Auscultation of lung sounds revealed coarse crepitation and rhonchi bilaterally. The patient did not have any dysmorphic facial features or skeletal deformities on exam. Neurological examinations were normal.

**Diagnosis/Assessment**

Complete blood count showed leukocytosis (WBC 36,230 per mm$^3$; neutrophils 27 %, lymphocytes 58 %, monocytes 13 %). Biochemical studies revealed normal plasma glucose (106 mg/dL), low serum calcium (5.8 mg/dL), normal serum phosphorus (5.2 mg/dL), and magnesium (1.8 mg/dL). Serum parathyroid hormone was elevated (117.7 pg/mL). Serum 25-hydroxyvitamin D (25(OH)D) was undetectable (<3 ng/mL). Serum alkaline phosphatase was normal for age (240 U/L). Serum electrolytes and kidney function were normal. A radiograph of the chest revealed perihilar infiltration. The respiratory panel result was positive for respiratory syncytial virus (RSV). Computer tomography of the brain and the cerebrospinal fluid profiles were normal.

The history of fever-provoked seizure in exclusively breastfed infant coupled with laboratory values that showed hypocalcemia, elevated PTH, and undetectable 25(OH)D level was consistent with the diagnosis of hypocalcemia due to severe vitamin D deficiency. The cause of fever, from the investigations, was consistent with RSV bronchiolitis.
Management/Outcome

Immediate treatment of severe vitamin D deficiency with symptomatic hypocalcemia requires intravenous calcium, oral calcitriol (the hormonal form of vitamin D, 1,25-dihydroxyvitamin D), and oral vitamin D supplementation. In this case, 10% calcium gluconate 1 mL/kg was promptly given intravenously every 6 hours along with oral calcitriol 1 mcg/day, oral calcium containing 500 mg of elemental calcium/day, and oral vitamin D$_2$ 10,000 IU/day. Phenytoin was also administered to control the seizure. Two days after treatment, his serum calcium increased to 7.2 mg/dL. Intravenous calcium was then decreased to 1 mL/kg every 12 hours. Four days after treatment, his serum calcium increased into the normal range (8.4 mg/dL). Intravenous calcium was then discontinued and his calcium remained in the normal range (8.8 mg/dL). Oral calcitriol was eventually decreased to a dose of 0.25 mcg/day on day 8 of treatment. His seizure ceased within the first day of starting treatment. He remained on calcitriol 0.25 mcg/day, calcium which contains 500 mg of elemental calcium/day, and vitamin D$_2$ 10,000 IU/day until day 10 of treatment and was then discharged home with oral vitamin D$_3$ 1400 IU/day and 300 mg of elemental calcium/day. Laboratory tests prior to discharge revealed normal calcium (10 mg/dL), normal phosphorus (4.7 mg/dL), and slightly elevated PTH (83.6 pg/mL). After his discharge to home, he went back to his home country and planned a follow-up visit at his home country.

Literature Review

Vitamin D sources in early infancy come from transplacental stores, breast milk, and cutaneous production via sunlight exposure. Maternal vitamin D status is important in determining the vitamin D reserves at birth via placental vitamin D transport and early infancy via breast milk. It is well recognized that maternal vitamin D deficiency during pregnancy and during lactation contributes to the development of vitamin D deficiency and rickets in infancy.
Exclusively breastfed infants of mothers who avoid sunlight and have inadequate vitamin D intake, similar to this case presentation, put their child at risk for developing vitamin D deficiency [1, 2].

The 2010 Institute of Medicine (IOM) recommends a daily vitamin D intake of 400–600 IU/day in pregnant women to achieve the circulating 25(OH)D of 20 ng/mL [3], whereas the Endocrine Society recommends an intake of 1500–2000 IU/day to achieve a circulating 25(OH)D level of more than 30 ng/mL [4]. There are many studies indicate that routine use of prenatal vitamins containing 400 IU of vitamin D does not prevent vitamin D deficiency in pregnant women [5–7]. The Endocrine Society recommends that all pregnant women should take at least a prenatal vitamin containing 400 IU vitamin D per day with a supplement that contains at least 1000 IU vitamin D per day. Studies of vitamin D supplementation in pregnancy showed that at least 1000–2000 IU/day of vitamin D may be needed to ensure serum 25(OH)D above 20 ng/mL [6, 8]. Two recent RCT showed that vitamin D intake of 4000 IU/day during pregnancy was most effective in achieving serum 25(OH)D concentrations of 32 ng/mL or more throughout pregnancy without increase risk of toxicity in pregnant women and their neonates [7, 9].

Post-partum during lactation, the Endocrine Society recommends that women should take at least a multivitamin containing 400 IU vitamin D along with at least 1000 IU vitamin D supplement every day. In women who exclusively breastfeed, at least 4000–6000 IU/day of vitamin D may be necessary to transfer adequate vitamin D into milk to satisfy the infant’s vitamin D requirements. Thus, at minimum, lactating women may need to take vitamin D 1400–1500 IU/day, and to satisfy their infant’s requirement, and they may need 4000–6000 IU/day if they choose not to give the infant a vitamin D supplement [4]. A RCT study in lactating women reported that daily vitamin D intake at the dose of 2000 and 4000 IU could achieve sufficient circulatory 25(OH)D level (>30 ng/mL) for mothers. However, infants of mothers ingesting 4000 IU/day of vitamin D exhibited higher 25(OH)D concentrations than infants of mothers ingesting 2000 IU/day of vitamin D [10]. A more recent study showed that a maternal intake vitamin D of 6400 IU/day during lactation was safe and significantly elevates circulating 25(OH)D level in both mothers and nursing infants. These results compared favorably with infants receiving 300–400 IU/day of vitamin D [11].
Human breast milk and unfortified cow’s milk contain very little vitamin D naturally. The average amount of vitamin D in human milk and colostrums is approximately 15.9 ± 8.6 IU/L [10]. Thus, infants who are fed only human breast milk are prone to developing vitamin D deficiency. The Endocrine Society recommends that infants require at least 400 IU/day of vitamin D to maximize bone health. However, to ensure blood levels of 25(OH)D consistently above 30 mg/dL, infants may require at least 1000 IU/day of vitamin D [4]. The American Academy of Pediatrics (AAP) recommends that all breastfed infants, infants who receive a mixture of human milk and formula milk, and any infant who receives <1 L or 1 qt of formula per day need vitamin D supplement of 400 IU/day beginning within the first few days of life and continuing throughout childhood to maintain serum 25(OH)D concentration at >20 ng/mL [12].

Despite daily supplementation with 400 IU as recommended by the AAP guidelines, vitamin D deficiency in infancy is still highly prevalent [13]. Some studies suggested that vitamin D supplementation in infants should be increased above the recommended 400 IU/day especially in winter season and in infants who have high risk of vitamin D deficiency such as in infants born to vitamin D-deficient mothers due to low sunlight exposure, low intake of dairy products, and inadequate vitamin D supplementation during pregnancy and lactation [14–16]. A recent RCT showed that vitamin D supplementation up to 1600 IU/day in infants was safe and resulted in serum 25(OH)D concentrations within the normal range and consistently above 32 ng/mL [16].

**Clinical Pearls and Pitfalls**

- Vitamin D status of infants is dependent on the mother’s vitamin D status early in life.
- Exclusively breastfed infants are at risk for developing vitamin D deficiency since very little vitamin D is contained in breast milk, especially if the mother is vitamin D deficient.
- Supplementation of the infant and of the lactating mother are two approaches to improve vitamin D status of children in early infancy.
Suggested Reading


References

Vitamin D
A Clinical Casebook
Tangpricha, V. (Ed.)
2016, IX, 102 p. 1 illus., Softcover
ISBN: 978-3-319-26174-4