Case Report

A late-preterm infant with hypocalcemic tetany caused by traditional soy milk feeding: A case report and literature review

Shu-Wei Hu[1,2,3*]

[1]Division of Pediatric Gastroenterology, Department of Pediatrics, Tungs' Taichung MetroHarbor Hospital, [2]Ph.D Program in Translational Medicine, [3]Rong Hsing Research Center for Translational Medicine, National Chung Hsing University, Taichung, Taiwan

Abstract

Hypocalcemia may cause numerous symptoms, including neuromuscular irritability, prolonged QT interval, apnea, cyanosis, tachypnea, vomiting, or laryngospasm. Here, we reported a late-preterm 3-month-old infant presenting general involuntary twitches caused by hypocalcemic tetany. Laboratory data revealed hypocalcemia–hyperphosphatemia, high parathyroid hormone, normal magnesium, and low vitamin D(25-OH). Calcium intake deficiency was suspected. The infant was cured after calcium supplementation through the intravenous route and standard infant formula.

Keywords: Hypocalcemia, infant, nutrition, soy milk

Introduction

Hypocalcemia is defined as a total serum calcium level of <7 mg/dL in preterm infants and <8 mg/dL in term neonates.[1] Early-onset hypocalcemia occurs within the first 72 h of life and is often asymptomatic, whereas, late-onset hypocalcemia occurs after the first 72 h and toward the end of the first week of life and is usually symptomatic. Symptoms associated with hypocalcemia include neuromuscular irritability, prolonged QT interval, apnea, cyanosis, tachypnea, vomiting, or laryngospasm.[1]

Healthy-term infants reach a physiological nadir in serum calcium levels by 24–48 h of age, and the serum calcium levels may be lower in high-risk neonates, including infants of mothers with diabetes, preterm, and perinatal asphyxia.[1] The calcium level is regulated by parathyroid hormone (PTH)-related peptide in fetus, and the calcium level depends on PTH secretion, dietary calcium intake, renal reabsorption, skeletal stores, and vitamin D status.[1]

The nutritional requirement of calcium was higher in late-preterm infants than in full-term infants because their bones contain smaller mineral stores. The calcium requirement was approximately 120–140 mg/kg/day for gestational age of 34–36 weeks and 70–120 mg/kg/day for full-term infants.[2] The recommended dietary allowance of calcium for 0–6-month-old infants was 200 mg/day by the American Academy of Pediatrics, and 300 mg/day by the Taiwan Food and Drug Administration.[3,4] Infants who do not meet the daily calcium intake recommendation may present hypocalcemia-associated manifestations or even death.

Herein, we report a late-preterm 3-month-old infant presenting general involuntary twitches. A further investigation proves that the traditional soy milk that did

Received: 15-Feb-2022, **Revised:** 12-Mar-2022, **Accepted:** 15-Mar-2022, **Published:** 26-Sep-2023.

Access this article online

Quick Response Code:

Website: https://journals.lww.com/TMJ

DOI: 10.4103/ETMJ.TMJ-111006

Address for correspondence: Dr. Shu-Wei Hu, Division of Pediatric Gastroenterology, Department of Pediatrics, Tungs' Taichung MetroHarbor Hospital, No. 699, Sec. 8, Taiwan Blvd., Wuqi Dist., Taichung 43503, Taiwan.
E-mail: t13223@ms3.sltung.com.tw

How to cite this article: Hu S-W. A late-preterm infant with hypocalcemic tetany caused by traditional soy milk feeding: A case report and literature review. Tungs Med J 2023;17:S42-4.

not contain enough calcium caused her hypocalcemic tetany.

Clinical Case

A 3-month-old (postmenstrual age of 49 weeks and 3 days) female infant was born at a gestational age of 35 weeks and 3 days with a birth body weight of 2724 g (75–90th percentile). No abnormal findings were observed in the prenatal examination, with no specific family histories such as thyroid disease or DiGeorge's disease. The mother did not have gestational diabetes mellitus, preeclampsia, hypercalcemia, or hyperparathyroidism, but maternal vitamin D status was unknown. After birth, she was fed with infant formula within 1 month of age. Neonatal jaundice was noted at 10 days of age, which was relieved after phototherapy and adequate feeding. No medication intake histories were traced. The baby was exclusively fed on traditional soy milk at 180–200 mL/5 h/day. Traditional soy milk was regularly purchased from a restaurant when the baby was 1 month old. Her parents preferred that kind of milk because they thought the soy milk was healthier for their baby. Decreased appetite and activity had occurred for 3 days before admission. Frequent general and focal tonic seizures with upward gazing were found for 2 h, and each seizure persisted for approximately 10 min. Increased muscle tone and poor weight gain (4.2 kg, 3–10th percentile) were found. Laboratory data revealed total serum calcium of 4.4 mg/dL, phosphorus of 8.0 mg/dL, magnesium of 1.7 mg/dL, alkaline phosphatase of 1041 U/L, intact PTH of 130.6 pg/mL, vitamin D(25-OH) of 9.9 ng/mL, and albumin of 3.8 g/dL. The cerebrospinal fluid analysis revealed negative findings. The cardiac sonography demonstrated an atrial septal defect and no coarctation of the aorta. The electroencephalography revealed normal findings. The serum calcium level 6 h after intravenous calcium chloride (20 mg/mL) administration at 4 mL increased from 4.4 to 5.1 mg/dL. Vitamin D was prescribed, and she was fed with standard infant formula since the second day of admission. Her serum calcium level was gradually corrected, and no seizure recurred. The serum calcium level was 7.7 mg/dL before discharge, and she was discharged with a full recovery. A 2-month follow-up laboratory data revealed calcium, phosphorus, intact PTH, and vitamin D(25 OH) levels within a normal range at 9.8, 5.6 mg/dL, 44.2 pg/mL, and 24.9 ng/mL, respectively.

Discussion

Many causes induced late-onset hypocalcemia in infants, such as increased phosphate load, hypomagnesemia, vitamin D deficiency, PTH resistance, hypoparathyroidism, metabolic syndromes, or iatrogenic causes.[1] Lee *et al.*[5] reported five infant cases with late-onset hypocalcemia caused by transient pseudohypoparathyroidism due to delayed renal maturation or magnesium deficiency.

Calcium concentrations in human milk vary from 25 to 35 mg/dL.[6] The standard infant formula contained 35–54 mg/dL of calcium and 70–80 mg/dL in the postdischarge formula.[3] The bioavailability of calcium was higher in human milk than in low birthweight formula.[7] The lactose-containing formula could increase the percentage absorption of calcium compared with the lactose-free formula, but the mechanisms are not fully understood.[8]

Traditional soy milk contained approximately 13 mg/dL of calcium, so it could not satisfy the daily calcium requirement of infants. Anil *et al.*[9] reported one 14-week-old infant with hypocalcemia–hyperphosphatemia due to soy milk feeding, with similar initial laboratory profiles as our case. Traditional soy milk was different from soy-based protein formula. Phytic acid is found in soybeans as phytin salts, which do not exist in humans and can chelate a series of minerals, including zinc, calcium, magnesium, and iron. Hence, soy-based protein formula was added with additional phosphorus and calcium of approximately 20% higher than those in cow's milk formula. The clinical role of soy-based protein formula was used in infants with severe cow's milk protein allergy.

Body calcium exists in two major compartments: skeleton (99%) and extracellular fluid (1%), and the skeletal calcium stores were less in preterm infants.[1,2,10] The bone mineralization was rapidly improved during the first months of life, and the preterm infants reached healthy terms between 6 and 12 months of age.[10] Bone turnover was stimulated after birth, and calcium and phosphorous would be released into the mineral pool.[2] The need for exogenous calcium was higher in preterm infants because the skeletal calcium sores were less than in term infants.

Here, the data revealed hypocalcemia–hyperphosphatemia, high PTH, normal magnesium, and low vitamin D(25-OH). However, vitamin D deficiency is usually presented with elevated PTH and normal or low serum inorganic phosphorus levels. Hence, calcium intake deficiency or high-phosphate load was considered the possible cause, and these could be differentiated by calculating the fractional excretion of inorganic phosphorus (FEiP). A high phosphate load was more likely if the FEiP was elevated. The drawback of this case report is that we did not check urine creatinine and urine phosphate with the onset of her symptoms. In addition, the baby had been exposed to traditional soy milk, and her blood test revealed hypocalcemia. Evidence supports that these two events are highly connected to each other. Therefore, primary caregivers and practitioners should keep in mind that

a history of traditional soy milk consumption may be important to the diagnosis of this condition when they are facing any infants presenting involuntary twitches, because severe hypocalcemia may cause neuromuscular and cardiac problems and even death.

Declaration of patient consent

The author certify that he have obtained appropriate patient's guardian consent form. In the form, the guardian has given the consent for the child's images and other clinical information to be reported in the journal. The guardian understands that the child's name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Data availability statement

All data generated or analyzed during this study are included in this published article.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1 Jain A, Agarwal R, Sankar MJ, Deorari A, Paul VK. Hypocalcemia in the newborn. Indian J Pediatr 2010;77:1123-8.
2 Lapillonne A, O'Connor DL, Wang D, Rigo J. Nutritional recommendations for the late-preterm infant and the preterm infant after hospital discharge. J Pediatr 2013;162(3 Suppl):S90-S100.
3 Golden NH, Abrams SA. Committee on nutrition. Optimizing bone health in children and adolescents. Pediatrics 2014;134: e1229-43.
4 Shaw NS, Hsu SC. Dietary Reference Intakes for Calcium, Iodine, Vitamin D, and Carbohydrate. 8th ed. Taiwan: Healthy Promotion Administration; 2020.
5 Lee CT, Tsai WY, Tung YC, Tsau YK. Transient pseudohypoparathyroidism as a cause of late-onset hypocalcemia in neonates and infants. J Formos Med Assoc 2008;107:806-10.
6 Jenness R. The composition of human milk. Semin Perinatol 1979;3:225-39.
7 Salle BL, Putet G. Calcium, phosphorus and vitamin D requirements in premature infants. In: Salle BL, editor. Nutrition of the Low Birth Weight. Nestle´ Nutrition Workshop Series, Belgium; 1993. p. 125-35.
8 Abrams SA, Griffin IJ, Davila PM. Calcium and zinc absorption from lactose-containing and lactose-free infant formulas. Am J Clin Nutr 2002;76:442-6.
9 Anil M, Demirakca S, Dotsch J, Kiess W. Hypocalcemia–hyperphosphatemia due to soy milk feeding in early infancy. Klin Pädiatr 1996; 208:323-26 [In Germanese: English abstract].
10 ESPGHAN Committee on Nutrition, Aggett PJ, Agostoni C, Axelsson I, Curtis MD, Goulet O, Hernell O, *et al*. Feeding preterm infants after hospital discharge. JPGN 2006;42:596-603.