Benign Neonatal Shudders, Shivers, Jitteriness, or Tremors: Early Signs of Vitamin D Deficiency

Millicent Collins, MD, Michal Young, MD

abstract

Jitteriness and tremors in the newborn period typically precipitate an extensive, invasive, and expensive search for the etiology. Vitamin D deficiency has not been historically included in the differential of tremors. We report a shivering, jittery newborn who was subjected to a battery of testing, with the only biochemical abnormality being vitamin D deficiency. A second case had chin tremors and vitamin D deficiency. Review of our patients suggests that shudders, shivers, jitteriness, or tremors may be the earliest sign of vitamin D deficiency in the newborn. Neonates who present with these signs should be investigated for vitamin D deficiency.

Shudders, shivers, jitteriness, and tremors are terms used to describe excessive movements in neonates. These terms, although used interchangeably, are defined variably, depending on the author. Jittery is a term used to describe a series of recurrent tremors in infants. Tremors are involuntary, rhythmic, oscillatory movements of equal amplitude. Tremors are described as fine or coarse. A fine tremor is of high frequency (>6 cycles per second) and low amplitude (<3 cm). Coarse tremors are of low frequency (>6 cycles per second) and high amplitude (>3 cm).[1] Shudders and shivers have a more colloquial usage. Meriam-Webster's dictionary describes a shudder as the act of trembling convulsively or shaking because of fear or cold. A shiver is described as a momentary trembling movement. Regardless of the term used, if repetitive and recurrent, such movements in the newborn period typically precipitate a search for the etiology among possibilities, such as hypoglycemia, hypocalcemia, hypothermia, hyperthyroidism, hypomagnesemia, drug withdrawal, sepsis, seizure, or neurologic disorder. Vitamin D deficiency has not been historically included in the differential of such movements; however, vitamin D deficiency is common in pregnant women (5% to 50%) and in breastfed infants (10% to 56%), despite the widespread use of prenatal vitamins, because these may be inadequate to maintain normal vitamin D levels (≥32 ng/mL).[2] We report 2 jittery newborns with the only biochemical abnormality being vitamin D deficiency. Review of our patients suggests that shudders, shivers, jitteriness, or tremors may be among the earliest signs of vitamin D deficiency in the newborn.

CASE 1

Past History

LB's mother (G2, P1) presented for a prenatal visit in her ninth month of pregnancy. She had no complications during this pregnancy, but complained that the prenatal vitamins had made her sick throughout her entire pregnancy. She did not drink milk. LB's mother was a dark-skinned

Department of Pediatrics, Howard University College of Medicine and Hospital, Washington, District of Columbia

Dr Collins provided 1 case report, drafted the initial manuscript, and reviewed and revised the manuscript: Dr Young conceptualized this case report, provided 1 case report, and reviewed the manuscript; and both authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

DOI: https://doi.org/10.1542/peds.2016-0719

Accepted for publication Jan 19, 2017

Address correspondence to Millicent Collins, MD, Department of Pediatrics, Howard University Hospital, 2041 Georgia Ave, NW, Washington, DC 20060. E-mail: m_collins@howard.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

To cite: Collins M and Young M. Benign Neonatal Shudders, Shivers, Jitteriness, or Tremors: Early Signs of Vitamin D Deficiency. *Pediatrics*. 2017;140(2):e20160719

native of Barbados and had lived for 15 years in Washington, DC, which is located at latitude 38° N. There were no cultural or religious reasons that would limit the mother's exposure to the sun. She had successfully breastfed her first child for 1 year while in Barbados.

Birth History

LB was born via normal spontaneous vaginal delivery at term in the month of August. Birth weight was 7 pounds, 2.2 ounces, length 20.5 inches, head circumference 35 cm. He was in the nursery for 3 days, had mild jaundice (bilirubin 8.1), and was totally breastfed. His mother expressed no difficulties relevant to breastfeeding.

Postnatal Visits

At age 6 days, on the initial ambulatory newborn visit, the mother's only concern was that LB seemed to shiver a lot "like he was cold." She noted that she lived in a basement apartment where her husband and her other child (age 2 years) often felt cold and sometimes shivered. The pediatrician counseled the mother about dressing an infant for a cool, damp environment. Just before leaving the office, the mother remembered that she had seen the tremors in the nursery but on questioning the staff about it, she had been told that it was normal. The mother assured the pediatrician that she was continuing to take her prenatal vitamins. During the physical examination, no tremors or shaking were noted.

At the age of 12 days, LB was brought by his mother for a follow-up visit. She noted that the tremors were worse. Indeed, on physical examination, the infant would periodically shiver as if cold. Even his head would shake. However, he remained alert and appropriately responsive. Mother would wrap him tightly, noting that while wrapped she continued to feel his movements. Because of the severity of his shaking, he was sent to the emergency department for evaluation. Vital signs remained normal for age. LB was afebrile and continued to be alert and interactive. Laboratory studies were done. These included complete blood count, comprehensive metabolic panel, magnesium, phosphorus, urine for toxicology, urinalysis, and thyroid function. See Tables 1, 2, and 3 for results. Urinalysis and thyroid function were normal.

Consultation with the neurology department was obtained. The neurologist noted that the head and body were shaking rhythmically at intervals lasting 2.0 to 2.5 minutes. Shaking was not related to crying or nasal regurgitation. Other segments of developmental and behavior evaluation were appropriate. On

TABLE 1 Results of Comprehensive Metabolic Panel in Case 1

	Result	Normal Range
Sodium, mEq/L	138	135–148
Potassium, mEq/L	5.2	3.5–5.3
Chloride, mEq/L	105	95–111
HCO2-, mEq/L	24	25–32
Glucose, mg/dL	116	70–115
Serum urea nitrogen, mg/dL	6	6–25
Creatinine, mg/dL	0.4	0.7–1.4
Calcium, mg/dL	10.7	8.5–10.6
Phosphorus, mg/dL	6.5	2.5–4.5
Magnesium, mg/dL	2.7	1.7–2.5
Total bilirubin, mg/dL	1.8	0.2–1.2
Aspartate amino transferase, U/L	28	0–50
Alanine amino transferase, U/L	11	0–55
Alkaline phosphatase, U/L	430	30–165
Total protein, g/dL	6.1	6–8.5
Albumin, g/dL	3.9	3.2–5.5

TABLE 2 Results of Complete Blood Count in Case 1

White blood cell	$11.5 \times 10^3/\mu L$
Red blood cell	$4.14 \times 10^6/\mu L$
Hemoglobin, g/dL	14.5
Hematocrit, %	41.3
Mean corpuscular volume, fL	99.7
Mean corpuscular hemoglobin, pg	35.1
Mean corpuscular hemoglobin concentration, g/dL	35.2
Red blood cell distribution width, %	15.6
Platelet count	$339 \times 10^3/\mu L$
Neutrophil, %	14.6
Lymphocyte, %	66.5
Monocyte, %	14.3
Eosinophil, %	2.8
Basophil, %	1.9

TABLE 3 Results of Urine Drug Screen in Case 1

Drug	Result
Amphetamine	Negative
Barbiturates	Negative
Cocaine	Negative
Methadone	Negative
Opiates	Negative
Benzodiazepines	Negative
Marijuana	Negative
Propoxyphene	Negative
Phencyclidine	Negative

physical examination, the infant was noted to have normal sutures and normal neonatal reflexes with excellent Moro and traction. The infant fixated and briefly followed. Good head control was noted. Asymmetrical tonic neck reflex was negative. Landau, grasp, Galant, support, and March reflexes were normal. Cranial nerves II to XII were normal. Motor evaluation revealed mild increase in tone of the lower extremities recurring periodically. Spontaneous movements also were noted. Evaluation of reflexes revealed mild hyperreflexia of all extremities: ankle clonus 4 to 5 beats sustained over 7 to 8 repetitions. Tremors were present at rest and in absence of excitation also involving the head and were not exaggerated or precipitated by crying or movement. It was also confirmed that tremulous muscular activity continued regardless of swaddling. Other clinical features of the tremors (frequency, distribution, amplitude, duration) were not measured numerically. Computed tomography of the brain was normal. EEG was recommended but the mother did not return at the appointed time.

The initial workup revealed a tremulous infant with laboratory studies that were all within normal limits, except for alkaline phosphatase of 430 μm. This was followed up with studies on mother and infant for 25 hydroxy vitamin D. Results for infant: 6 ng/mL (normal 30–100). Studies were not available for the mother at the same time.

The infant was recalled to start vitamin D at 800 IU daily. When the mother was told the results, she admitted that she had not taken any prenatal vitamins ever. She was successfully breastfeeding her infant and was not supplementing with formula. She was not giving vitamins to the infant. Mother's vitamin D was not available until day 65 of life: 22.5 ng/mL (normal = 30–100).

Within 2 weeks, after starting treatment, LB's tremors had subsided completely.

CASE 2

Baby Boy VR was delivered via normal spontaneous vaginal delivery in the month of October, to a 20-year-old, dark-skinned African American primigravida, after an uncomplicated pregnancy in Washington, DC. Apgar scores were 9 and 9 at 1 and 5 minutes, respectively. Mother had fair prenatal care beginning at the fifth month of pregnancy. She took prenatal vitamins during her pregnancy. After delivery, the infant's examination was remarkable only for occasional shudder of the infant's chin. Glucose screening was normal. Vitamin D level was done and the level was 17 ng/mL. The infant was being formula fed. He was started on vitamin D at 800 IU daily. He was referred to his pediatrician for follow-up care. No further information was available for this infant.

DISCUSSION

The classification of neonatal tremors is not as clearly defined as the case for childhood and adult tremors. Additional terms, such as shudders, shivers, or jitteriness, are often applied. These terms seem to be used interchangeably with tremors. Tremors may be defined as an involuntary, rhythmic, periodic, mechanical oscillation of a body part.[1,3] Riehl and Mink[4] described shuddering as brief episodes of shivering-like movements of the head, shoulders, and arms. Basheer[5] defines jitteriness as tremor of variable amplitude and frequency, involving the jaw and extremities.

Neonatal tremors in otherwise healthy newborns have largely been assumed to be a benign neonatal characteristic that resolves spontaneously after a few months of life.[4–7] Isolated tremors presenting within the first few days from birth are generally considered benign or physiologic, and generally disappear within days.[7] However, when tremors persist, and/or exacerbate, more serious diagnoses are often considered. These include seizures, neurologic abnormality, hypoglycemia, hypocalcemia, hypomagnesemia, hyperthyroidism, drug withdrawal, and sepsis. Leone et al[7] followed 84 low-risk infants in Rome, Italy, with persistence of tremors after the first week. Initial evaluation was done to exclude the previously mentioned more serious diagnoses but did not include alkaline phosphatase or vitamin D levels. No mention was made of feeding and nutrition, making the role of vitamin D indeterminable in this study. They concluded that neonatal tremors can have a variable evolution and resolution. All infants were healthy at the age of 24 months.[7] Relative to etiology, Leone et al[7] proposed the possibility of transient immaturity, defects at the level of supraspinal organization, and circulating catecholamines,[7] all of which indicate the need for additional study, but dietary considerations are obviously absent.

Our patients initially exhibited tremors within the first 2 days of life. Case 1 presented in the office at the age of 6 days with "shivers" that had been noted in the nursery and again at the age of 12 days with obvious worsening. Most descriptions of physiologic tremors do not indicate that worsening should be expected. In addition, the infant's mother was breastfeeding, she was not supplementing with formula, and she was not taking prenatal vitamins, hence her breast milk was a limited source of vitamin D. The workup was negative for the more common causes of tremors but with laboratory studies compatible with vitamin D deficiency. Notable in case 1 are several risk factors exhibited

by the mother: (1) dark skin, (2) refusal to take prenatal vitamins, (3) distaste for milk and milk products, (4) breastfeeding without taking prenatal vitamins, and (5) location in a low-sunlight latitude.[8,9] As the infant in case 1 was being breastfed without supplementation and the mother was not taking prenatal vitamins, the tremors were worsening. Improvement was not noted until the infant was receiving supplemental vitamin D. Had the infant been fed formula that contains vitamin D, it is possible that an apparent "spontaneous resolution" may have been ultimately noted after 4 to 6 weeks.

Case 2 exhibited chin tremors and the only pertinent abnormality was low vitamin D. In case 2, vitamin D levels were drawn because the authors had noted the tremors of case 1 and were curious as to what the vitamin D levels might reveal with this symptomatology. We were surprised to get this finding. Attempts to locate this dyad failed, as the mother did not keep the appointment with the community physician. Attempts to locate her through the Medicaid managed care insurer also failed; either she had changed insurers or moved out of the area. We included this case because of the surprised association with these subtle symptoms. Further studies will be needed to clarify this association more fully. Formula feeding would address this deficiency over time. However, as we are encouraging mothers to make a healthier feeding choice by breastfeeding their infants, physicians need to be aware of vitamin D levels in the face of this feeding choice. Further, the maternal vitamin D deficiency is important to this mother's subsequent health, as vitamin D deficiency has been associated with hypertension.[10,11]

It is well known that above the latitude of 37° N, an individual's skin makes lesser amounts of vitamin D from the sun. Both mothers had lived in latitude 38° N during their pregnancies. Although the infants were born during the late summer/early fall, outdoor activities were likely limited in the third trimester of pregnancy. Considering that both mothers had dark skin, maternal production of vitamin D could be expected to be low.

Currently, the American Academy of Pediatrics recommends exclusive breastfeeding of infants. The Academy also recommends that, while doing so, vitamin D supplementation of these infants should start soon after delivery. Recognizing the reality that mothers may not be adherent in taking prenatal vitamins or supplementing infants, practitioners who care for children should equally advocate the importance of supplementing vitamin D for these infants.

The degree of hypovitaminosis D appears related to variable symptomatology. Case 1 had a low vitamin D level and significant clinical manifestations. This level is in the range in which an infant without supplementation and without sufficient sun exposure can develop clinical signs of rickets. The infant in case 2 had chin tremors with a higher vitamin D level of 17 ng/mL and much milder symptoms, but still recognizable as abnormal.

Clinical manifestations of vitamin D deficiency are related to calcium and bone metabolism. It has been recognized that low calcium can cause general neuromuscular excitability but the mechanism of this paradox remains elusive.[12] However, early vitamin D deficiency may occur with a normal calcium. Perhaps, in the early stages of vitamin D deficiency, neuronal excitability is elicited by changes at the level of intracellular calcium and cannot be detected by current testing methods.

Yorifuji et al[13] suggest that the earliest sign of vitamin D deficiency is craniotabes. Craniotabes, like tremors in otherwise healthy newborns, has largely been regarded as a physiologic condition without the need for treatment. In this study, healthy Japanese neonates were checked for craniotabes at 5 to 7 days as part of routine discharge. Twenty-two percent were found to have craniotabes. Yorifuji et al[13] did not address the presence or absence of abnormal movements, specifically, jitteriness, tremors, shivers, or shudders, in their study population. On recheck at 1 month, craniotabes persisted in approximately one-third. Laboratory evaluation of these infants showed statistically significant elevations in serum alkaline phosphatase with slightly more than one-third having 25 OH vitamin D <10 ng/mL. Early evidence of vitamin D deficiency was detected in both the Japanese patients and our patients within the first week of life. More research will be needed to determine if one precedes the other or perhaps both may present simultaneously as early signs of vitamin D deficiency.

CONCLUSIONS

Benign newborn tremors may not always be benign. The assumption that neonatal tremors, in the otherwise asymptomatic healthy-appearing neonate, are benign, may be incorrect. Neonatal tremors may be among the earliest clinical signs of vitamin D deficiency. Consequently, vitamin D deficiency should be considered in the workup of tremors in the term neonate who has no other indicators of pathology. Additional study is needed to solidify this apparent relationship.

REFERENCES

1. Armentrout DC, Caple J. The jittery newborn. *J Pediatr Health Care*. 2001;15(3):147–149
2. Mulligan ML, Felton SK, Riek AE, Bernal-Mizrachi C. Implications of vitamin D

deficiency in pregnancy and lactation. *Am J Obstet Gynecol*. 2010;202(5):429.e1–429.e9

3. Habib-ur-Rehman. Diagnosis and management of tremor. *Arch Intern Med*. 2000;160(16):2438–2444
4. Riehl JA, Mink JW. Shuddering attacks. *J Pediatr Neurol*. 2010;8:25–27
5. Basheer SN. Neonatal jitters. *J Pediatr Neurol*. 2010;8:5–6
6. Fernandez-Alvarez E. Polymorphic, benign, nonepileptic, paroxysmal, infantile movements (Fejerman condition). *J Pediatr Neurol*. 2015;13(04):231–236
7. Leone D, Brogna C, Ricci D, et al. Development of clinical signs in low risk term born infants with neonatal hyperexcitability. *Early Hum Dev*. 2013;89(2):65–68
8. Dawodu A, Wagner CL. Mother-child vitamin D deficiency: an international perspective. *Arch Dis Child*. 2007;92(9):737–740
9. Williams AF. Vitamin D in pregnancy: an old problem still to be solved? *Arch Dis Child*. 2007;92(9):740–741
10. Forman JP, Scott JB, Ng K, et al. Effect of vitamin D supplementation on blood pressure in blacks. *Hypertension*. 2013;61(4):779–785
11. Reeves IV, Bamji ZD, Rosario GB, Lewis KM, Young MA, Washington KN. Vitamin D deficiency in pregnant women of ethnic minority: a potential contributor to preeclampsia. *J Perinatol*. 2014;34(10):767–773
12. Han P, Trinidad BJ, Shi J. Hypocalcemia-induced seizure: demystifying the calcium paradox. *ASN Neuro*. 2015;7(2)
13. Yorifuji J, Yorifuji T, Tachibana K, et al. Craniotabes in normal newborns: the earliest sign of subclinical vitamin D deficiency. *J Clin Endocrinol Metab*. 2008;93(5):1784–1788