Dizziness and Fainting in an 8-Year-Old Girl

Kevin Couloures, DO, MA
Rukmani S. Vasan, MD, MPH, FAAP

CASE PRESENTATION

History

An 8-year-old girl whose family recently immigrated to the United States from Mexico was brought to the emergency department (ED) by her mother because of a 1-day history of dizziness and fainting. The mother spoke no English and only elementary Spanish. She reported with difficulty through an interpreter that her daughter was standing on the patio the previous day when her legs collapsed under her own weight. The child required her mother's assistance to stand for 2 minutes before she could stand on her own. The child did not feel dizzy or light-headed during the episode, and she felt fine 10 minutes later. She remained well until the morning of presentation, when she experienced a second episode.

Five days earlier, the child had had a fever associated with a brief period of stiffening and then trembling. During the episode, there had been no jerking movements, and her eyes had not rolled back. She had not lost consciousness and had experienced no bladder or bowel incontinence; she had had no headache or feeling of sleepiness after the event. Paramedics had been called and had taken the child to a hospital, where her condition had been diagnosed as febrile seizures; she had been discharged home after 4 hours of observation.

The child had received a diagnosis of speech delay at age 3 years and had undergone subsequent speech therapy. Her mother also reported that her daughter had had a febrile seizure 1 year ago when they still lived in Mexico. The child's birth history was normal, with no prior hospitalizations or surgeries. Her vaccination history was up to date, except for varicella immunization.

Key Point

Seizure and syncope can be difficult to differentiate from one another. Paying close attention to the symptoms preceding and following the event can be quite useful in distinguishing these two entities. Seizures frequently are associated with aural symptoms prior to the event and are followed by a postictal alteration in the mental state.[1] The increasing frequency of syncopal events requires prompt evaluation. Infectious agents, recurrent intoxication, and an intracerebral mass or hemorrhage should all be strongly considered.

Physical Examination

On examination, the girl was alert, was awake, and appeared comfortable. The following vital signs were obtained: oral temperature, 37.1°C (98.7°F); heart rate, 64 bpm; respiratory rate, 20 breaths/min; blood pressure, 103/64 mm Hg. The child's height was 150 cm (59 in), and her weight was 59 kg (130 lb), both in the 99th percentile for age. Her speech was difficult to comprehend. During the routine blood pressure examination, the examiner noted a carpal spasm. Neurologic examination showed diminished deep tendon reflexes at the biceps, patella, and ankle with normal muscle tone and strength. Trousseau's phenomenon and Chvostek's sign were both present. The remainder of the physical examination was unremarkable. The child was in the Tanner I stage of pubertal development. Thickening of the wrists and ankles, brachydactyly, or dysmorphic features were not observed.

Dr. Couloures is a Resident Physician, Internal Medicine and Pediatrics combined program at Los Angeles County/University of Southern California Medical Center, Los Angeles, CA. Dr. Vasan is an Assistant Professor of Clinical Pediatrics, Keck School of Medicine, University of Southern California; and the Director of Pediatric Primary Care and the Associate Program Director, Medicine/Pediatrics Residency Program, Los Angeles County/University of Southern California Medical Center, Los Angeles, CA. Dr. Giardino is the Vice President for Clinical Affairs and the Associate Chair of Pediatrics, St. Christopher's Hospital for Children, Philadelphia, PA; and a member of the Hospital Physician *Editorial Board. Dr. Pasquariello is the Director of the Diagnostic Center, Division of General Pediatrics, Department of Pediatrics, Children's Hospital of Philadelphia, Philadelphia, PA.*

Table 1. Initial Laboratory Values of Case Patient

Variable	Result	Normal Range
Hematologic values		
Leukocyte count	$7.1 \times 10^3/mm^3$	$3.4–10.8 \times 10^3/mm^3$
Differential		
Segmented neutrophils	42%	40–60%
Lymphocytes	45%	20–40%
Platelet count	$282 \times 10^3/mm^3$	$227–539 \times 10^3/mm^3$
Hemoglobin	13.3 g/dL	12.0–14.5 g/dL
Serum values		
Blood urea nitrogen	8 mg/dL	7–22 mg/dL
Electrolytes		
Sodium	141 mEq/L	135–148 mEq/L
Potassium	4.4 mEq/L	3.5–4.1 mEq/L
Chloride	102 mEq/L	96–109 mEq/L
Bicarbonate	28 mEq/L	24–30 mEq/L
Calcium	5.3 mg/dL	8.0–10.5 mg/dL
Magnesium	1.7 mg/dL	1.3–2.0 mg/dL
Phosphate	9.7 mg/dL	3.2–6.3 mg/dL
Albumin	3.9 g/dL	3.4–5.4 g/dL
Ionized calcium	2.5 mg/dL	4.52–5.28 mg/dL
Serum creatinine	0.7 mg/dL	0.3–0.7 mg/dL

Key Point

The abnormal neurologic findings discussed above strongly suggest hypocalcemia as a possible cause of seizures or syncope. Any focal neurologic deficit, change in mental status, or significant head trauma would warrant an emergent computed tomography (CT) scan of the head.[2] However, most children with seizures will have normal results on physical examination.[3] The examiner should carefully note any dysmorphic features, which may suggest a congenital infection or genetic abnormality.

Laboratory Studies

Results of laboratory studies of blood taken in the ED are summarized in **Table 1**. A lumbar puncture was not performed because the patient was afebrile with a normal sensorium; the neck was supple, and no focal deficits were noted on examination. The peripheral leukocyte count and differential also did not suggest infection.

Key Point

The patient's severe hypocalcemia and hyperphosphatemia require urgent treatment and work-up to prevent cardiac arrhythmia and neurologic sequelae.

DIFFERENTIAL DIAGNOSIS

A child with seizures or syncope needs prompt initial evaluation to ensure that the airway, breathing, and circulation are stable. Once the child's condition is stable, a more accurate history and thorough physical examination can occur. An accurate history can be challenging to obtain, as exemplified by this case in which the child's mother had difficulty clearly describing the events, and the child had a speech impediment. When a parent cannot clearly describe the event, it may be helpful to have him or her imitate the event.

Seizures have a U-shaped incidence, occurring primarily in the pediatric and geriatric age groups. More than 50% of seizures are idiopathic, but it is important

to exclude treatable causes of seizure.[3] A significant cause of seizures in children is infection, which, in the appropriate clinical setting, warrants a lumbar puncture to exclude meningitis. Meningitis presents as new onset seizure in 20% to 30% of pediatric cases, and the seizure can be focal or generalized. The most common causative agent of meningitis in the pediatric age group is *Neisseria meningitidis*.[4] This child was afebrile on presentation without clinical signs of infection; therefore, an infectious etiology was less likely. However, the diagnosis of febrile seizures was also inappropriate because the child was not within the diagnostic age range of 6 months to 6 years.[5,6] Febrile seizures typically occur early in the onset of febrile diseases.[5]

Cysticercosis was also considered in the differential diagnosis because the child came from Mexico, where *Taenia solium*, the causative agent of cysticercosis, is endemic. The ingested eggs have an incubation period that can last from months to years; therefore, the infection may present long after the patient has emigrated from the endemic region.[7] Cysticercosis can be identified with CT imaging of the head, which would show a solitary parenchymal cyst with or without contrast enhancement and numerous calcifications.

The late age of onset of the patient's episodes lowers the likelihood of inborn errors of metabolism (eg, pyridoxine dependency, maple syrup urine disease, hyperglycinemia) or other amino and organic acid disorders. Carbon monoxide poisoning or another recurring intoxication (eg, hypoglycemic drugs, alcohol) could also initially present as syncope or seizures but is unlikely in an otherwise well-appearing child. Metabolic imbalances such as hypoglycemia, electrolyte imbalances, hypoxemia, uremia, and hyperammonemia should always be considered in pediatric patients with seizures.

Syncope can be confused with a seizure, because a syncopal episode may trigger symptoms that can be diagnosed as a seizure. The absence of prodromal or postictal symptoms in the patient's history most likely suggest syncope rather than seizures as the diagnosis. The syncopal evaluation should focus on excluding cardiac abnormalities as the underlying etiology. Therefore, it should be determined whether the patient has had any prior syncopal events or cardiac surgery and whether any first-degree relatives have experienced syncopal events or sudden death. The examiner should also note whether the syncope was exercise-related and whether the patient experienced chest pain or palpitations.[8] An electrocardiogram (ECG) is useful for screening for arrhythmias, such as those that occur in Wolff-Parkinson-White syndrome,

heart block, and long QT syndrome, as well as for hypertrophic cardiomyopathies and myocarditis.[9]

Although it is important to exclude cardiac causes of syncope, the most common etiology of syncope in the pediatric patient is a vasovagal reaction. The vasovagal reaction, known as *neurally mediated syncope*, is mediated by an alteration in the patient's systemic vascular tone. Orthostatic blood pressure and heart rate measurements can help determine whether hypovolemia or decreased peripheral tone is responsible for the syncopal episode.[10] If the patient is experiencing multiple syncopal episodes or finds them particularly troubling, a head-upright tilt-table test may be useful in diagnosing the underlying etiology. Although most syncopal episodes are benign, children with these episodes should be followed for at least 1 year because a syncopal episode can be the presenting sign of a seizure disorder.[11]

CLINICAL COURSE

The patient was admitted to the hospital for observation during correction of her hypocalcemia and for further evaluation. An initial ECG performed in the ED showed QT prolongation (**Figure 1**). The patient was placed on a continuous cardiac monitor and given a 2-g bolus of calcium gluconate intravenously over 1 hour. Following a pediatric endocrinology consultation, additional laboratory studies, including evaluation of thyroid function, vitamin D levels, and parathyroid hormone (PTH) levels, were performed (**Table 2**). Oral calcium replacement therapy was initiated in the form of calcium carbonate 1800 mg (720 mg elemental calcium) taken 3 times daily. The patient also began taking calcitriol 0.5 μg twice daily. One day after admission, her serum ionized calcium level had increased to 3.40 mg/dL, with resolution of her symptoms. Results of chromosomal studies (ie, karyotype analysis, fluorescence in situ hybridization) were normal. A CT scan of the head revealed extensive areas of calcification in the globus pallidus, putamen, and subcortical frontal and parietal lobes consistent with a metabolic disorder (**Figure 2**). Ultrasonography of the kidneys showed no masses or calcifications.

On hospital day 4, the patient's serum calcium level normalized at a value of 8.9 mg/dL. Thyroid-stimulating hormone (TSH) and vitamin D levels were both within normal limits; however, the intact PTH level was markedly decreased. Results on an antimicrosomal antibody test were negative, and no other endocrine abnormalities were detected. She continued her calcium carbonate and calcitriol therapy with close monitoring of her symptoms and was discharged on hospital day 5.
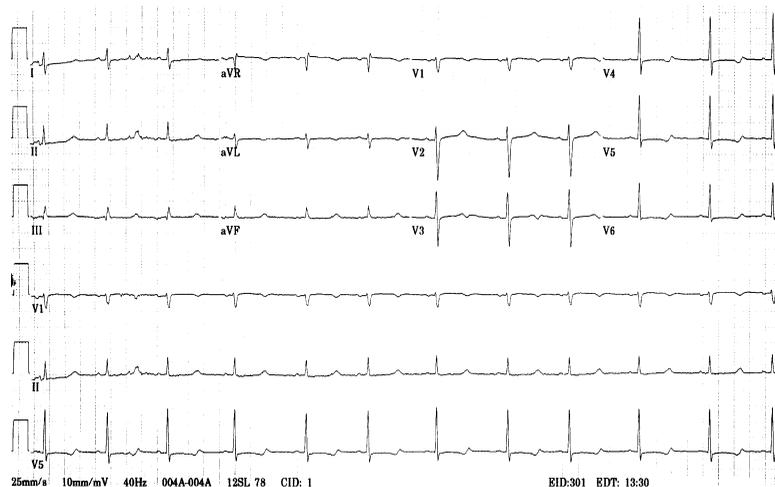
Figure 1. Electrocardiogram of the case patient showing QT prolongation.

The patient has not experienced any further seizures or syncopal episodes during the past year and attends special education classes. No thyroid, adrenal, or pancreatic disorder has manifested itself to date.

HYPOPARATHYROIDISM
Definition

PTH and vitamin D are the major regulators of calcium homeostasis. Absent or abnormally low levels of PTH result in hypocalcemia and hyperphosphatemia. A related abnormality, pseudohypoparathyroidism (Albright's hereditary osteodystrophy) occurs when the parathyroid gland functions normally, but a defect in the receptor for the adenylate cyclase system prevents normal calcium regulation.

Pathophysiology

PTH acts directly on the bone and kidney and indirectly on the intestines to maintain a normal serum ionized calcium level. PTH induces the distal tubule of the nephron to reabsorb calcium and enhances the excretion of phosphate. PTH also acts upon the kidney to induce the hydroxylation of 25-hydroxycholecalciferol to 1,25-dihydroxycholecalciferol. The 1,25-dihydroxycholecalciferol then acts upon the intestine to promote the absorption of calcium from ingested food. In the bone, PTH stimulates the osteoclasts to break down the cellular matrix, releasing calcium into the blood. 1,25-Dihydroxycholecalciferol has a similar effect on the osteoclasts, but the onset of action is slower than that of PTH. The PTH level is regulated primarily by the serum ionized calcium level, but it also can be affected by the serum magnesium level. Therefore, the serum magnesium level must always be normalized when treating hypocalcemia.

Epidemiology

Hypoparathyroidism is a rare disorder with an equal incidence in males and females. The aplasia or hypoplasia of the parathyroid glands that occurs in DiGeorge syndrome affects 1 in 10,000 newborns.[12] In Japan, the prevalence of idiopathic hypoparathyroidism is approximately 7.2 (5.5–8.8) per million, and the prevalence of pseudohypoparathyroidism is approximately 3.4 (2.6–4.2) per million, with similar rates expected in the United States.[13]

Etiology

Transient hypocalcemia occurs in infants born to mothers who have an undiagnosed parathyroid adenoma, but the condition usually resolves by the third week of life and requires no further treatment. Besides genetic and autoimmune causes, the major etiology of hypoparathyroidism is excision or damage during thyroidectomy. Genetic disorders that can cause hypoparathyroidism include DiGeorge syndrome, Kearns-Sayre syndrome, and other inherited defects. DiGeorge syndrome and velocardiofacial syndrome have been correlated with deletions in the 22q11 chromosome.[14] The autoimmune-mediated disease known as autoimmune polyendocrinopathy–candidiasis–ectodermal dystrophy (APECED) syndrome affects multiple organs; frequently, its primary manifestation is hypocalcemia. APECED is an autosomal recessive mutation in the autoimmune regulator gene.[15]

Clinical Presentation

Symptoms in children with hypoparathyroidism may range from none to seizures and mental retardation. A low serum calcium level may be well compensated and clinically undetected until a child hyperventilates or

Table 2. Results of Endocrinology Laboratory Studies of the Case Patient

Variable	Result	Normal Range
Thyroid-stimulating hormone	2.22 µU/mL	0.6–6.3 µU/mL
Vitamin D		
1,25-Dihydroxycholecalciferol	41 pg/mL	15–90 pg/mL
25-Hydroxycholecalciferol	25 ng/mL	17–54 ng/mL
Intact parathyroid hormone	< 2 pg/mL	10–65 pg/mL

becomes febrile.[16] Early signs of hypocalcemia include muscle fatigue and cramps, which then progress to numbness, stiffness, and tingling of the hands or feet. Later signs include laryngeal or carpopedal spasms. Convulsions and mental retardation are the result of longstanding or severe hypocalcemia.

Physical Examination

In patients with hypoparathyroidism, the skin is frequently dry and scaly; these symptoms persist following correction of the calcium level. The teeth may be hypoplastic, aplastic, or late in eruption. Cataracts may be present in patients with chronic hypocalcemia, and a slit-lamp examination is necessary to rule out their presence. Signs of congestive heart failure, including hypotension, bradycardia, and cardiomegaly, also may be present.

Diagnosis

A low serum calcium level with a concurrent high-normal or elevated serum phosphorus level raises the likelihood of a diagnosis of hypoparathyroidism. Evaluation of 25-hydroxycholecalciferol and 1,25-dihydroxycholecalciferol levels should be performed to exclude vitamin D deficiency, which induces hypertrophy of the parathyroid gland, increasing PTH levels. Normal serum calcium levels are maintained at the expense of decreased phosphorus reabsorption and hypophosphatemia. Thyroid function also should be evaluated by measuring TSH levels and free thyroxine uptake. Subclinical hypothyroidism occurs in pseudohypoparathyroidism and may only be detected by the presence of an elevated TSH level. Immunometric determination of the PTH level is the definitive test, once other causes of hypocalcemia have been excluded.[17]

Radiography of the long bones may show extremely dense bones. Skull radiography may show hypoplastic or aplastic teeth. CT of the head may reveal calcifications of the basal ganglia, particularly in patients with longstanding hypocalcemia. Ultrasonography of the kidneys also should be performed to evaluate the presence of nephrocalcinosis.
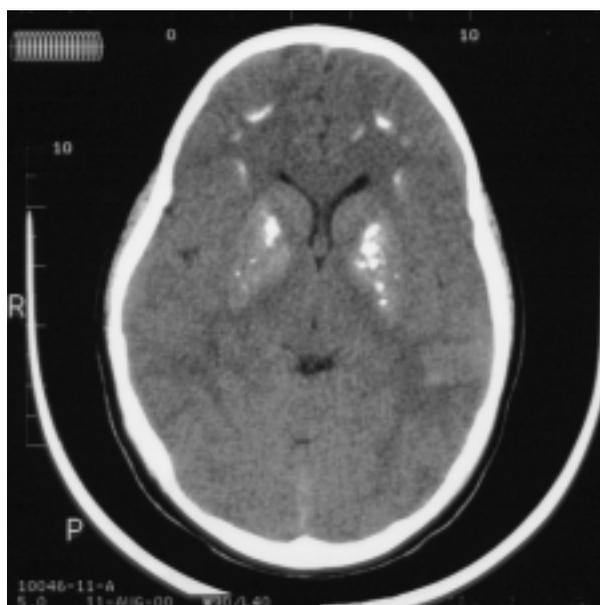

Figure 2. Computed tomography scan of the head of the case patient revealing extensive calcifications in the globus pallidus, putamen, subcortical frontal lobe, and parietal lobe of the brain.

In patients with hypoparathyroidism, an ECG will show a prolongation of the QT interval, which is corrected when the serum calcium level returns to normal.

Treatment

The first goal in the treatment of patients with hypoparathyroidism is rapid correction of the serum calcium level to prevent seizures or cardiac arrhythmia. The patient should be placed on a cardiac monitor while calcium gluconate is infused intravenously. The patient should then be started on daily calcium supplements, and calcitriol should be administered twice daily. The goal of therapy is a serum calcium level greater than 7.5 mg/dL. Serum and urine calcium and phosphorus levels should be routinely monitored to achieve low-normal calcium levels. Increased urine calcium levels may require an alteration in management to prevent

the formation of renal stones. Treatment of hyperphosphatemia is rarely needed. If hypercalcemia does occur, withholding the calcitriol for 3 to 4 days usually resolves the condition. Maintenance of normal serum calcium levels prevents tetany and cardiac side effects, but it does not reverse the cerebral calcifications.[18]

CONCLUSION

This child's case highlights the challenges in differentiating seizures from syncope in a pediatric patient. Observation of the carpal spasm led the physician to measure the patient's serum calcium level immediately. Subsequently, the evaluation focused on the cause of the child's hypocalcemia. No nutritional deficiencies or excess phosphate ingestion were identified from the patient's history, and the initial laboratory study results did not suggest any renal pathology. The low level of PTH with no other endocrine abnormalities suggested idiopathic hypoparathyroidism or the initial stage of APECED. Close follow-up will be essential to maintain the patient's low-normal serum calcium level and monitor for the development of other endocrinopathies associated with APECED. **HP**

REFERENCES

1. Vedanarayanan VV. Diagnosis of epilepsy in children. Pediatr Ann 1999;28:218–24.
2. Berg AT, Testa FM, Levy SR, Shinnar S. Neuroimaging in children with newly diagnosed epilepsy: a community-based study. Pediatrics 2000;106:527–32.
3. Nigro MA. Seizures and status epilepticus in children. In: Tintinalli JE, Kelen GD, Stapczynksi JS, editors. Emergency medicine: a comprehensive study guide. 5th ed. New York: McGraw-Hill; 2000:825–38.
4. van Deuren M, Brandtzaeg P, van der Meer JW. Update on meningococcal disease with emphasis on pathogenesis and clinical management. Clin Microbiol Rev 2000;13:144–66.
5. Hirtz DG. Febrile seizures. Pediatr Rev 1997;18:5–8, quiz 9.
6. Haslam RHA. The nervous system, febrile seizures. In: Behrman RE, Kliegman RM, Jenson HB, editors. Nelson textbook of pediatrics. 16th ed. Philadelphia: WB Saunders; 2000:1818–9.
7. Pickering LK, Peter G, Baker CJ, et al. 2000 Red book: report of the Committee on Infectious Diseases. 25th ed. Elk Grove (IL): American Academy of Pediatrics; 2000:560–2.
8. Walsh CA. Syncope and sudden death in the adolescent. Adolesc Med 2001;12:105–32.
9. Lewis DA, Dhala A. Syncope in the pediatric patient. The cardiologist's perspective. Pediatr Clin North Am 1999;46:205–19.
10. Johnsrude CL. Current approach to pediatric syncope. Pediatr Cardiol 2000;21:522–31.
11. Aysun S, Apak A. Syncope as a first sign of seizure disorder. J Child Neurol 2000;15:59–61.
12. Doyle DA, DiGeorge AM. Disorders of the parathyroid glands. In: Behrman RE, Kliegman RM, Jenson HB, editors. Nelson textbook of pediatrics. 16th ed. Philadelphia: WB Saunders; 2000:1715–8.
13. Nakamura Y, Matsumoto T, Tamakoshi A, et al. Prevalence of idiopathic hypoparathyroidism and pseudohypoparathyroidism in Japan. J Epidemiol 2000;10:29–33.
14. Greig F, Paul E, DiMartino-Nardi J, Saenger P. Transient congenital hypoparathyroidism: resolution and recurrence in chromosome 22q11 deletion. J Pediatr 1996; 128:563–7.
15. Marx SJ. Hyperparathyroid and hypoparathyroid disorders [published erratum appears in N Engl J Med 2001;344:240,696]. N Engl J Med 2000;343:1863–75.
16. Shaia HJ, Rahal F. Index of suspicion. Case 2 presentation. Pediatr Rev 1997;18:248–50.
17. Guise TA, Mundy GR. Clinical review 69: evaluation of hypocalcemia in children and adults. J Clin Endocrinol Metab 1995;80:1473–8.
18. Avioli LV. The therapeutic approach to hypoparathyroidism. Am J Med 1974;57:34–42.