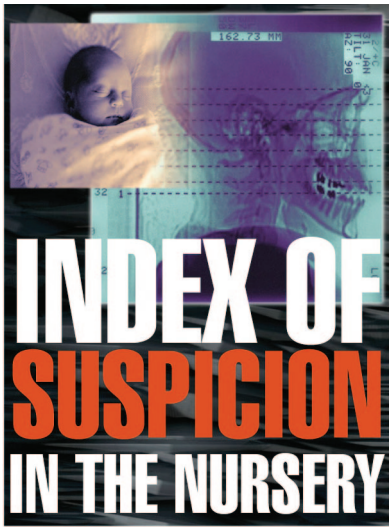

The reader is encouraged to write possible diagnoses for each case before turning to the discussion. We invite readers to contribute case presentations and discussions. Please inquire first by contacting **Dr. Philip at aphilip@stanford.edu.**

Author Disclosure

Drs Arbona, Diaz, and Scarano did not disclose any financial relationships relevant to this case.

Case Presentation

A 2-month-old male baby is admitted to the hospital for the third time with a history of abnormal movements since the first day after delivery. He returns to the hospital on this occasion due to the appearance of bluish skin associated with the occurrence of abnormal movements that persist despite the use of anticonvulsant medication.

The parents describe the abnormal movement as a sudden, startling jump followed by a forceful body contraction in which the baby becomes rigid, with fists firmly clenched, arms flexed, spine erect, head tilted slightly backward, and legs extended. He remains awake during and after the episode. The contraction lasts for approximately 10 seconds and is followed by floppiness for 1 to 2 seconds. Sometimes episodes are accompanied by a bluish coloration of the entire body. Startling sounds or even a sudden touch trigger the episodes, which occur frequently all day long. They explain that firm holding and hugging sometimes seem to stop the episodes.

On questioning, they report no eye rolling, blinking, or lip smacking during the episodes, and the episodes usually are not preceded by feedings. The boy has good suckling and appetite; no constipation or diarrhea; and is active, afebrile, and seemingly otherwise healthy.

A review of the pregnancy and delivery reveals no complications or infections during the pregnancy, although the mother says that the movements of the baby in the womb seemed different from those in previous pregnancies. At birth, the infant aspirated meconium, with associated respiratory distress. Apgar scores were 7 at 1 minute and 9 at 5 minutes. The infant was admitted to the neonatal intensive care unit (NICU) due to respiratory distress and received ampicillin and gentamicin, but he did not require intubation or blood transfusion.

Cultures of cerebrospinal fluid, blood, and urine were negative. ABO incompatibility was associated with indirect hyperbilirubinemia, which resolved with phototherapy.

He began having abnormal movements in the NICU, but results of electroencephalography (EEG), neurosonogram, and brain computed tomography (CT) scan were normal. He was discharged from the hospital with a prescription for oral phenobarbital. He was readmitted a few days later due to the persistence of symptoms, but EEG, brain CT scan, and metabolic test results still were normal. On subsequent hospital discharge, oral phenytoin was added to the anticonvulsant regimen.

There is no history of convulsive disorder in the family or any other significant disease in the parents and siblings.

On physical examination, the baby is awake and active, and vital signs are normal. He startles in reaction to clapping of the hands and tapping over the patellar tendon. The startle reaction is exaggerated, characterized by a jump followed by a generalized muscular spasm, with clenching of the fists, flexion of the arms, erection of the spine, and extension of the legs. As reported by the parents, there is no lip smacking, rolling of the eyes, or blinking. The episodes last a few seconds and can be stopped with forced flexion of the head and legs over the trunk. If the episodes are not stopped, baby's face turns cyanotic. He exhibits hypertonia during episodes.

His head circumference is 34 cm, and the fontanelles are neither bulging nor sunken. He has no hypo- or hyperpigmentation of the skin, no

hemangiomas, and no skin lesion. There is no palate deformity or dysmorphic facies. The heart beat is regular without a murmur. Breath sounds are normal, with bilateral clear lung auscultation. The abdomen is not distended, and there is an umbilical hernia. There is no acrocyanosis. Testicles are descended with hydrocele.

Neurosonography reveals no subependymal or intracranial hemorrhage, and periventricular echogenicity is normal. Results of head CT scan, brain magnetic resonance imaging (MRI), and EEG are normal. Blood culture is negative at 5 days, urine culture is negative at 48 hours, and results of urinalysis are within normal limits. Two measurements of ammonia are 34.3 mcg/dL (48 mcmol/L) and 28.0 mcg/dL (20 mcmol/L), glycine is minimally increased, lactic acid measurements are 31 mg/dL (3.4 mmol/L) and 0.6 mg/dL (0.07 mmol/L), pyruvic acid is less than 0.1 mg/dL (11.4 mcmol/L), total carnitine is 54 mcmol/L, and free carnitine is 54 mcmol/L. A human immunodeficiency virus-1 enzyme-linked immunoassay test result is negative, and the infant's blood type is B+.

The clinical findings coupled with the generally negative laboratory tests suggest the diagnosis.

Case Discussion

Differential Diagnosis

Tonic seizure is suggested by stiffening of muscles in this case, but there is no EEG abnormality, and tonic seizures are not sensory-induced. The seizures being induced by unexpected stimuli and a startle response followed by a tonic phase suggest the possibility of startle seizure, but there are no corresponding EEG abnormalities. Stiffening of the body also occurs in infantile spasm, but such spasms are not sensory-induced.

Diagnosis

Hyperekplexia is a nonepileptic disorder characterized by an exaggerated startle response and generalized muscular rigidity triggered by sensory stimuli. It is also known as stiff baby syndrome or startle disease.

Clinical manifestations can appear early in the prenatal period as abnormal intrauterine movements. In the postnatal period, it presents with increased muscle tone that may predispose to hernias and abnormal movements consisting of tonic spasms and myoclonus that may be associated with episodes of apnea. The clinical hallmark is flexor spasm induced by nasal bridge tapping.

The pathophysiology of hyperekplexia is impaired function of inhibitory neurotransmitters (glycine/GABA) related to glycine chloride channels mutation or autoimmune-mediated damage of glutamic acid decarboxylase.

Because hyperekplexia is not characterized by epileptiform discharges or structural brain anomaly, EEG, brain CT scan, and brain MRI yield normal findings. Nonetheless, electromyography discloses almost permanent muscular activity.

Among the complications are hernias, discomfort, and pain due to the hypertonic state, with episodes of apnea during tonic spasms that may be life-threatening. Mental retardation also may be associated with hyperekplexia.

The hypertonia may ameliorate spontaneously with increasing age, but it also may recur in adult life. Persistence of the exaggerated startle response may continue through adulthood, leading to falls. Delayed motor development may be seen.

This chronic condition has no cure and may alter the patient's lifestyle. Medical management is directed toward decreasing muscle tone with administration of clonazepam and forced flexion of the head and legs toward the trunk when the patient experiences the abnormal movement.

Lesson for the Clinician

Hyperekplexia is not a particularly common diagnosis, but knowing the features of its clinical presentation may enable the clinician to differentiate this disorder from epileptic disorders that may seem similar. Hyperekplexia should be considered in patients who experience abnormal movements triggered by sensory stimuli and in whom a tonic spasm can be elicited by tapping the nasal bridge. Other potential clues are stopping of the abnormal movements by maneuvers such as forced flexion of head and legs toward the trunk; normal results on cerebrospinal fluid analysis, EEG, brain CT scan, and MRI; and the presence of umbilical hernias due to hypertonicity and abnormal movements. Management involves knowing the maneuver that stops the spasm and, thus, prevents the associated apnea due to forceful tonic spasms. (*Ileana M. Arbona, MD, Tania Diaz, MD, Jenaro Scarano, MD, Department of Pediatrics, Saint Luke's Memorial Hospital, Ponce, Puerto Rico*)

Suggested Reading

Praaven V, Patole SK, Whitehall JS. Hyperekplexia in neonates. *Postgrad Med J.* 2001;77:570–572

Victor M, Ropper AH. Disorders of muscle characterized by cramp, spasm, pain, and localized masses. In: *Principles of Neurology.* 7th ed. New York, NY: McGraw-Hill; 2001:1569–1570

Nolte J. Drugs, diseases, and toxins can selectively affect particular parts of individual neurotransmitter systems. In: *The Human Brain: An Introduction to its Functional Anatomy.* 5th ed. St. Louis Mo: CV Mosby; 2002:192–193