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CASE REPORT

E.P.C.M.S.

A Case of Infantile Botulism

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BACKGROUND INFORMATION

Floppiness or hypotonia in an infant is a common clinical problem and may be associated with a wide range of unrelated disorders. It may be the presenting feature of a neuromuscular disorder; it may occur in the newborn period as a result of a perinatal insult to the central nervous system or may manifest later in infants with mental retardation or cerebral palsy. Hypotonia may also be a manifestation of a connective tissue disorder or could be associated with various metabolic disorders in infancy. Floppiness (or hypotonia) may be an incidental and nonspecific feature of an acutely ill child and it is completely physiologic in the premature infant (1-2). Recognizing hypotonia, even in early infancy, is usually relatively straightforward, but diagnosing the underlying cause can be difficult and often unsuccessful. Therefore, diagnosing the hypotonic infant is a very important issue. In the hypotonic infant, careful attention should be paid to the history and clinical examination, as one is likely to get more help from these in arriving at a diagnosis than from many of the more sophisticated and specialized investigations such as CT scans, MRI scans, EEG, blood tests, genetic testing (chromosome karyotypings and tests for specific gene abnormalities), spinal taps, electromyography muscle tests, or muscle and nerve biopsy.

CASE PRESENTATION

A 5 ½ months old male presented with 1 day history of fussiness, lethargy and taking longer to feed. He seemed sleepier and his parents noticed that his head was turned to one side. He had no fever, no coryza symptoms, no seizures, no vomiting, no change in bowel habits, no urinary symptoms and no sick contacts.

The patient's birth history was unremarkable. Growth and development were appropriate for age and immunizations were up to date. This infant was exclusively breastfed and just started being offered some solid foods. There was no family history of neurodevelopmental regression, musculoskeletal or metabolic diseases. He was admitted to the hospital for acute bronchiolitis at one month of age.

On admission, the infant was awake but somewhat lethargic, hypotonic, with head lag and weak cry. Basic laboratory tests as well as sepsis work-up including lumbar puncture were within normal limits.

Three days after admission, the patient became listless, drooling, with more profound hypotonia and was constipated. On the 5th hospital day, he became apneic and bradycardic and eventually was placed on mechanical ventilation. Further studies to rule out hypothyroidism, Guillain-Barre syndrome, metabolic disorders and tick bite were requested; all came back normal. Stool for Botulinum toxin was submitted.

The patient was weaned from mechanical ventilator 1 1/2 weeks after admission, when his motor function and respiratory effort gradually improved. He was not interested in breastfeeding after extubation but improved after a few days. Although the infant was moving his extremities, he continued to be hypotonic and with complete head lag. Patient's stool came back positive for botulinum toxin A. During that time, the infant was in stable condition and slowly but continuously improving. When he went home 2 weeks after admission, the patient's muscle tone was still decreased. He was sucking well and cough as well as gag reflex were present.

This patient was followed up closely by his general pediatrician and physical therapist. The infant's muscle tone showed gradual improvement. Two months later, there was good head control and with mild hypotonia. Patient could sit with support and was gaining weight appropriately well.

DISCUSSION

Hypotonia is not a specific medical disorder, but a potential manifestation of many different diseases and disorders that affect motor nerve control by the brain or muscle strength (3). Appropriate evaluation of an infant with hypotonia should start with getting detailed history. The history may provide a clue to the time of onset of the symptoms, such as our case which is acute hypotonic case. This helps us narrow down our differential diagnosis to meningitis (bacterial or viral), Guillain-Barre syndrome, tick bite, botulism, poliomyelitis, or porphyrias.

Botulism is a rare but potentially life-threatening neuroparalytic syndrome resulting from the action of a neurotoxin produced by Clostridium botulinum (4). Initially, infant botulism appeared to be most prevalent in California, Utah, and southeastern Pennsylvania. Currently, cases are being reported throughout the United States, the United Kingdom, Australia, Canada, and Asia (4). The classic clinical manifestation is an afebrile infant less than 6 months old who has constipation and generalized weakness manifested by poor head control, poor suck, and weak cry. Primary risk factors include the ingestion of honey and living in

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a rural area. There is also a high incidence of breast feeding in infants with botulism, although a causal connection has not been established (5).

The symptom complex is caused by ingesting *Clostridium botulinum* spores, which colonize the gut and produce a neurotoxin. A definitive diagnosis is made by isolating the organism or the toxin from the stool (5-6). An electromyographic pattern of brief small-amplitude potentials is characteristic but not diagnostic. The initial diagnoses considered most often are sepsis and meningitis. It is important to rule out these entities with appropriate blood work and a spinal tap because aminoglycosides, which often are used empirically, may potentiate the toxin. Myasthenia gravis also is considered frequently but can be differentiated by the use of edrophonium testing and the persistence of pupillary light and deep tendon reflexes, which disappear in botulism. Guillain-Barre syndrome is rare in children less than 6 months of age. It can be differentiated from botulism by an elevated cerebrospinal fluid protein and electromyographic patterns of denervation and prolonged nerve conduction velocity. Poliomyelitis may cause symmetrical paralysis without fever or meningeal signs, but unlike botulism, there are leukocytes in the cerebrospinal fluid. Dehydration, electrolytes derangement, Reye syndrome, cerebrovascular accident, and toxic exposures (including organic phosphates, heavy metals, and carbon monoxide) should be considered (7).

Diagnosis of botulism is the isolation of C. botulinum toxin from stool. The initial detection of the toxin requires one to four days. Electromyography (EMG) findings consistent with infant botulism are not pathognomonic and are described as short-duration, low-amplitude motor unit potentials, and repetitive nerve stimulation at rates of 20 to 50 Hz with an abnormal incremental response. An incremental response to 50 Hz stimulation is seen in 92 percent of infants with botulism poisoning, compared with 20 percent of normal infants.

Treatment with human-derived botulinum immune globulin (called BIG-IV or Baby BIG) is available for intravenous use in infants less than one year of age who are diagnosed with infant botulism. Treatment should not be delayed while awaiting results of confirmatory tests. In our case, we did not provide BIG-IV after consulting with our specialist who suggested that there was no significant difference between supportive management and BIG-IV administration 14 days after the onset of symptoms.

Mortality in botulism ranges from less than 5 percent to 8 percent (including infants). The mortality rate for infant botulism, the most common form in the United States, is less than 1 percent (8).

REFERENCES

1. Volpe, JJ. Neurological examination: normal and abnormal features. In: Neurology of the Newborn, 4th Ed, WB Saunders, Philadelphia, 2001. p.103.

2. Axelrod, FB, Porges, RF, Sein, ME. Neonatal recognition of familial dysautonomia. J Pediatr 1987; 110:946.

3. Amiel-Tison, C, Grenier, A. Neurological assessment during the first year of life. Oxford University Press, New York 1986.

4. Kerner, J. Neue Beobachtungen uber die in Wurtemburg so haufig vorfallen Vergiftung durch den Genuss gerauchter Wurst. Tubingen, 1820. Quoted in: Damon, SR, Food Infections and Food Intoxications. Williams and Wilkins, Baltimore 1928. p.67.

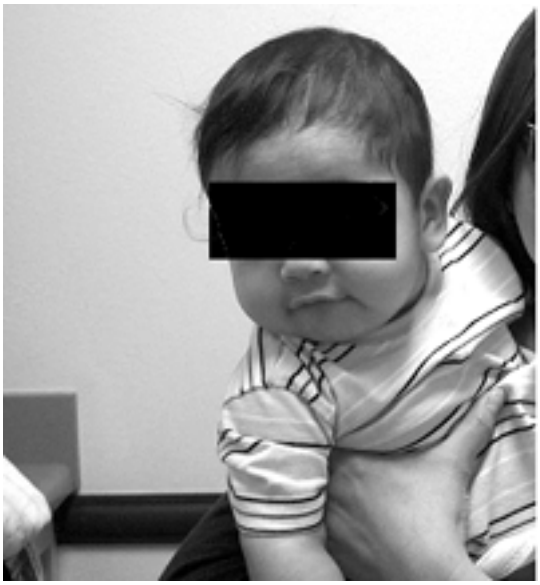
5. Sobel, J. Botulism. Clin Infect Dis 2005; 41:1167.

6. Roland, EH, Ebelt, VJ, Anderson, JD, Hill, A. Infant botulism: a rare entity in Canada?. CMAJ 1986; 135:130.

7. Sellin, LC. Botulism-an update. Mil Med 1984; 149:12.

8. Arnon, SS, Schechter, R, Maslanka, SE, et al. Human botulism immune globulin for the treatment of infant botulism. N Engl J Med 2006; 354:462.

Pictures 1 and 2



Two months after discharge, our patient (here at age 7 months) was followed up at TT clinic. He had good head control and was mildly hypotonic. He could sit steadily for 15 seconds without support. He was sucking fairly well and gained weight appropriately for his age

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