Amon

Early severe infantile botulism

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Two neonates with a history of diarrhea, abrupt apnea, and suspected sepsis were proved to have infantile botulism. Initial symptoms in both infants suggested other diagnoses. Electrophysiologic studies were important in confirming the diagnosis. Early severe infantile botulism may be rare but should be considered in neonates who have hypotonia and respiratory arrest or a sepsis-like clinical picture. (J PEDIATR 1993;122:909-11)

Even classic infantile botulism, because of its subacute onset, may be difficult to recognize.[1,2] Characteristically, infantile botulism occurs in previously healthy infants between 2 and 6 months of age.[1] After a period of constipation, hypotonia, ptosis, impaired sucking, decreased respiratory function, and dilated pupils, respiratory arrest and death may occur.[2,3] Although rare cases of neonatal botulism have been noted, these cases have not been discussed individually.[4-6] We have recently seen two neonates, aged 11 and 13 days, with acute onset of paralysis and respiratory arrest. Both patients proved to have early severe infantile botulism or "neonatal botulism."[7]

CASE REPORT

Patient 1. A 13-day-old white female infant was transferred from an outlying hospital after having a respiratory arrest. The infant was born at term to a 16-year-old single mother with an uneventful pregnancy and delivery. Birth weight was 3.1 kg. This infant had been fed since birth with standard formula containing iron. There was no exposure to honey or syrup. The mother lived with her parents. The grandfather, a meat inspector, inspected stockyards, feeding lots, and meat-processing plants. The patient's symptoms began with a 24-hour period of diarrhea and vomiting. She was seen by a local physician and given a 12.5 mg promethazine suppository and discharged. While en route home she suddenly had a respiratory arrest. The emergency medical service personnel arrived by ambulance and found the infant to be cyanotic and pulseless. Tracheal intubation was performed with difficulty, but there was no subsequent difficulty in ventilating the infant's lungs. She was brought to the emergency department at the community hospital and given intravenous infusions of ampicillin, 200 mg/kg per day, and gentamicin, 10 mg/kg per day, after blood culture specimens were drawn and was then transferred by helicopter to our institution.

On arrival at the hospital, the infant was limp, pale, and unresponsive while undergoing assisted ventilation. Her pulse was 142 beats/min, ventilator rate was 44/min, temperature was 100.7° C (rectal), and blood pressure was 100/52 mm Hg. The anterior fontanelle was small and flat; pupils were equal, about 4 mm, and sluggish. No spontaneous eye opening was noted. Over the lungs, loose rhonchi were heard bilaterally. Neurologic examination showed marked generalized hypotonia and depression of all deep tendon reflexes. The cerebrospinal fluid had no leukocytes, no erythrocytes, and normal glucose and protein concentrations. Blood culture specimens were drawn and the child was given ampicillin, 100 mg/kg per day, and gentamicin, 5 mg/kg per day. On the third hospital day, gentamicin levels were measured; the peak level was 5.6 μg/ml and trough was 0.5 μg/ml (both therapeutic, nontoxic levels). Ventilatory support was continued. Cultures of cerebrospinal fluid, blood, and urine and initial stool culture exhibited no growth. The electroencephalogram and computed tomographic scan were normal.

Because of the severe hypotonia, an electromyogram was performed on the ninth hospital day. This study demonstrated "significantly low amplitude responses," so a diagnosis of infantile botulism was entertained. Stools were collected for botulin toxin and antibiotic therapy was discontinued. The state laboratory isolated and confirmed the presence of *Clostridium botulinum* toxin, type B, by gelatin hydrolysis. *C. botulinum* was also isolated from two stool specimens by anaerobic culture on cooked meat medium with dextrose and starch and by chemical fermentation studies at our laboratory. The infant required ventilation for 23 days before she was weaned from the ventilator. Seven days after the first electromyogram was obtained, a second electromyogram showed a low-amplitude pattern with normal motor conduction velocities. Dur-

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ing the remaining 22 days of hospitalization, the infant slowly gained strength and at the time of discharge was feeding by nipple, was gaining weight normally, and had minimal hypotonia.

Patient 2. An 11-day-old infant was transferred by helicopter from a different outlying hospital with a history of 24 hours of refusing feedings and of loose stools, followed by an apneic spell. The infant was born at term to a 22-year-old woman after an uneventful pregnancy and delivery; birth weight was 3.5 kg. This infant had been fed human milk exclusively since birth. The family lived in a small rural town and the father was an oil-field worker; his company had recently been drilling for oil and natural gas. The parents denied having observed previous respiratory difficulty, fever, or constipation. About 2 hours before transfer, a parent reported that the infant was found in her crib with apnea and cyanosis. She was then taken to the emergency department at the local hospital, where tracheal intubation was required. Studies for sepsis consisted of a spinal tap, which was traumatic, and a blood culture. The infant was given ampicillin, 100 mg/kg per day, and gentamicin, 15 mg/kg per day, and transferred to our institution.

On arrival at our institution, the infant was given ventilatory support. She was found to be flaccid, hypotonic, and pale with inadequate respiratory effort; her pupils were 3 mm and sluggish. No spontaneous eye opening was noted. The infant's heart rate was 160 beats/min, her respiratory rate was 30/min (by ventilator), and her temperature was 97.8° C (axillary). Blood, spinal fluid, and urine cultures were negative for pathogens. The computed tomographic scan and electroencephalogram were normal. Because the physical findings were similar to those of patient 1, antibiotic therapy was stopped (only one dose of gentamicin was given, and that was before transfer; no levels were obtained). A pediatric neurologist was consulted. The electromyogram demonstrated severe low-amplitude responses consistent with infantile botulism. Subsequently, stool specimens tested by a state laboratory confirmed type B botulin toxin by gel hydrolysis. Anaerobic stool cultures at our laboratory also confirmed the presence of *C. botulinum*. The infant required mechanical ventilation for 28 days. Her tone returned to normal before discharge. At a follow-up visit she had normal tone and was feeding well, gaining weight, and developing normally.

DISCUSSION

Our two patients had a distinctive clinical picture. At the onset of their symptoms, they were much younger than typical patients with infantile botulism.[1, 2, 6] Initial symptoms in both infants suggested other diagnoses, such as sepsis. Instead of constipation, both had loose stools. The onset of apnea was acute and occurred within 24 hours of the first symptoms. Sepsis was suspected in both infants, resulting in the use of antibiotics. Because aminoglycosides were used, neuromuscular blockade by the botulin toxin was probably potentiated.[4, 5] Both neonates continued a prolonged clinical course of apnea and hypotonia.[4, 8, 9] Because of the abrupt respiratory arrest that occurred in both patients, an anoxic insult was strongly suspected as the cause of the abnormal neurologic status. Only after normal electroencephalograms and computed tomographic scans were obtained was a neuromuscular cause of the apnea entertained.

The source of *C. botulinum* in both infants was believed to be soil contamination. The grandfather in the first case and the father in the second case were employed in jobs where there was dust exposure. In both cases soil was broken by either cattle or oil drilling, thereby aerosolizing the *C. botulinum* spores and contaminating the clothing of these men. The spores possibly were then brought home to the infants. Neither infant had exposure to honey or corn syrups, which have been associated with infant botulism.

No one has specifically discussed the acute onset or severity of infantile botulism occurring before 1 month of age.[1-9] Spika et al.[3] defined the risk factors but not the presentation or the severity of infantile botulism in patients less than 2 months of age. Of their 69 cases, 10 infants were less than 1 month of age, including one infant 6 days of age.[3] Schreiver et al.[6] also reported 57 patients with infantile botulism ranging in age from 18 to 219 days at the time of onset; constipation was noted in 65% of the infants, but not diarrhea, and only 11% had respiratory difficulties at the time of admission.[6] Graf et al.[5] described a 3-week-old infant who had loose stools and in whom sepsis was suspected; later in the hospital course, constipation and apnea developed. This single case was similar to ours but had less severe features.

Both of our infants had low-amplitude compound muscle action potentials and normal conduction velocities. Because botulism was suspected, both low-frequency (3 Hz) and high-frequency (20 Hz) repetitive stimulation was performed. As expected, 3 Hz stimulation showed a decremental response and 20 Hz stimulation showed an incremental response.[6] Electrophysiologic studies were instrumental in demonstrating the presynaptic block of neuromuscular transmission in our patients, as seen in botulism.[4, 6] Stool studies confirmed the presence of botulin toxin in our patients and will reduce the need for unnecessary investigations.[5, 8] A high index of suspicion is needed to recognize this syndrome at this very young age.

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Apnea in infantile botulism

To the Editor:

Hurst and Marsh (J PEDIATR 1993;122:909-11) described two cases of infantile botulism with apnea. However, in the first case, apnea rapidly followed the rectal administration of approximately 4 mg of promethazine per kilogram of body weight. Because of the close temporal association of the administration of the promethazine and the apnea, it appears that the early respiratory compromise of the underlying botulism was hastened by the promethazine. The authors, in a kindly fashion, refrained from commenting on the decision of the "local physician" to use a relatively large dose of promethazine in a newborn infant. Although this infant eventually required extended ventilatory support as a result of the botulism, it is worth noting that because of the potential for respiratory depression and apnea, promethazine is not recommended in the newborn period.[1] In older children the drug is used for nausea and vomiting in a dose of 0.25 to 0.5 mg/kg and for sedation as a single agent at 1 mg/kg.[2]

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Reply

To the Editor:

We did consider promethazine overdose initially in the diagnosis of respiratory arrest in the first patient. In fact, we initially attributed the respiratory arrest to promethazine administration. However, on further examination, because of the severe hypotonia and subsequent electromyographic findings and the eventual confirmation of botulism, we thought it might have contributed to, but was not the cause of, respiratory arrest. When the second infant had almost identical findings and had received no promethazine, we believed that promethazine may not have played a role. Therefore we chose not to emphasize it in our article.

We wish to correct a statement regarding the laboratory diagnosis of botulism. When one of us (D.H.) called to find out how the botulism toxin had been confirmed by the state laboratory, he was informed of the culture methods that are as stated in the article. However, the toxin type was eventually confirmed by the Texas State Laboratory by mice toxin injection and protection assay using polyvalent antitoxins.

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Pulsed dye laser therapy for port-wine stains in children

To the Editor:

As a pediatric anesthesiologist and a pediatric dermatologist with 3 years of experience in providing office anesthesia for laser therapy for port-wine stains, we share the following observations and comments:

The literature consistently refers to the pain caused by the pulsed dye laser as that of a "sharply snapping rubber band." Children without sedation uniformly find it unpleasant. With deep sedation or general anesthesia (without muscle relaxants), patients reflexly withdraw from the pain produced by the laser and have increases in blood pressure and heart rate. We believe that the degree of pain generated by this procedure is underestimated. In anesthetic terms, one mean alveolar concentration (MAC) is the concentration of an inhalation agent at which half of a sample of nonparalyzed patients undergoing surgical abdominal incision move in response to the incision. One MAC or more is frequently required to maintain stillness in a patient undergoing pulsed dye laser surgery. An abdominal incision and a snapping rubber band probably conjure up different degrees of pain in the minds of most pediatricians. In an era when pediatric anesthesia is being increasingly incorporated into the neonatal unit, the critical care unit, the pediatric emergency department, and the oncology unit, the arguments for withholding adequate analgesia for a painful procedure performed on a child appear abusive.

Strauss and Resnick (J PEDIATR 1993;122:505-10) stated that "the health and psychologic risks of giving general anesthesia repeatedly to young children are also unknown." We do not pretend to know the psychologic risks, but if "health" as used here refers to physical risks, there is ample literature to indicate that there are