

Two Cases of Infant Botulism Presenting with Altered Mental Status

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Abstract

Infant botulism is a progressive process described as starting with descending weakness, facial palsies and constipation. Loss of bulbar reflexes and flaccid paralysis are common in infants less than 6 months old who have infant botulism. Clostridium botulinum, the bacteria that produce the toxin that causes this condition, are ubiquitous in the United States including Hawai'i, but infant botulism is rarely reported here. This report describes 2 cases of infant botulism with atypical initial presentations diagnosed on O'ahu, Hawai'i. Patient A is a 3-month-old male who presented with altered mental status, including inconsolability, who progressed to loss of gag reflex and constipation. Due to early concern for meningitis, Patient A was treated with antibiotics, however further evaluation led to eventual positive testing for botulinum B toxin. Patient B is a 2-month-old female who presented with somnolence and fever after immunizations and progressed to respiratory failure and apparent dehydration. Because she presented shortly after receiving immunizations, metabolic disorders were strongly considered as a potential cause of symptoms, but Patient B had normal metabolic evaluation and eventually tested positive for botulinum A toxin. Altered mental status and fever are unusual presentations for infant botulism. Infant botulism should be considered in infants with altered mental status when the course of illness includes the development of constipation and weakness, and evaluations are not suggestive of alternative causes, including infection, metabolic diseases, and spinal muscular atrophy. Early consideration and treatment of infant botulism should be considered for infants presenting with altered mental status who develop neuromuscular weakness. The Infant Botulism Treatment and Prevention Program (www.infantbotulism.org) should be contacted early for assistance with diagnosis and treatment.

Keywords

Infant botulism

Abbreviations

CDC = Centers for Disease Control and Prevention

CSF = cerebrospinal fluid

ED = emergency department

IBTTP = Infant Botulism Treatment and Prevention Program

SMA = spinal muscular atrophy

Introduction/Background

Infant botulism, first described in 1977 as acute infantile motor unit disorder, is caused by a toxin produced by *Clostridium botulinum*.¹ The progression of infant botulism includes a 3-30 day incubation period followed by symmetric descending motor weakness, constipation, and cranial nerve palsies. Infant botulism has been described with a large variety of clinical presentations, most commonly hypotonia, flaccid paralysis, and loss of bulbar reflexes in infants less than 6 months of age.² It is an acute progressive condition that is not usually

associated with preceding febrile episodes nor altered mental status.² Infant botulism, unlike other forms, is caused by gut colonization with *C. botulinum* and can be transmitted by dust particles. Patients may not have a history of exposure to home canned foods or honey ingestion, which lead to food-borne botulism.³ Early diagnosis and treatment can markedly improve the natural history and recovery from infantile botulism.⁴ The challenge of treatment within Hawai'i is the delay in receiving the medication from the mainland.⁵ This report includes 2 cases of infant botulism with novel presentations and chief complaints of altered mental status and, in 1 case, fever.

The families of both patients presented provided consent for the use of their child's de-identified case information for both the purposes of education and publication. As no experimental treatments or protocols were used in either case, formal Tripler Army Medical Center Institutional Review Board approval was waived.

Case A Presentation

Patient A was a 3-month-old male who presented to the emergency department (ED) with inconsolability for 16 hours. His parents reported that the patient started vigorously crying the night prior and had not stopped for longer than 10 minutes since that time. The parents also reported decreased oral intake and low urine output. Patient A had been healthy except for congestion, which had improved from the preceding week. Initial concern was for meningitis due to inconsolability, and cerebrospinal fluid (CSF) and blood were obtained. Broad spectrum antibiotics were started. Initial studies revealed no abnormalities consistent with infection in blood or CSF culture, complete blood count, complete metabolic panel, or CSF glucose levels, protein levels, or gram stain. The patient was admitted and cultures remained negative. With negative infectious work up and persistent marked irritability, metabolic disease screening was initiated, but serum lactate, ketones, ammonia, and pyruvate were normal for age. On day 2 of the hospitalization, the patient became increasingly hypotonic with decreased gag reflex. Subsequently, he was transferred to the Pediatric Intensive Care Unit and intubated for airway protection. Over the next 2 days he developed constipation and had decreasing peripheral reflexes. Given the evolving symptoms, infant botulism was considered and the team contacted the California Department of Public Health's Infant Botulism Treatment and Prevention Program (IBTTP; www.infantbotulism.org) who provided botulism immune globulin (intravenous human) (brand name BabyBIG).⁶

Confirmatory stool testing was completed and found positive for botulinum toxin B. The patient started to have spontaneous movements within 4 days of administration and was extubated after a total of 19 days. Patient A was discharged with minimal clinical deficits after a 5-week hospital course.

Case B Presentation

Patient B, a previously developmentally normal and healthy 2-month-old female, presented to the ED with fever up to 102°F as well as decreased feeding and activity that had started within hours of routine immunizations. On exam, she was markedly somnolent with hypertension and decreased response to painful stimuli. Initial concerns were for sepsis, dehydration, and encephalopathy. Infusion of crystalloid fluid boluses to correct poor perfusion due to early sepsis or dehydration did not improve her mental status. CSF, blood and viral cultures, C-reactive protein, and a complete blood count were obtained, and all were normal. A cerebral fetal monitor was placed to assess for any seizure activity, and brain magnetic resonance imaging obtained. Both tests had normal results. Ophthalmologic exam was normal. The patient developed respiratory failure due to hypoventilation 3 days after admission and was intubated. Metabolic testing revealed normal lactate, liver enzymes, and ammonia levels. The patient developed progressive peripheral hypotonia and loss of gag reflex on day 4 of hospitalization and was given a dose of botulism immune globulin on day 6 of her hospitalization after consultation with IBTPP.⁶ Stool testing confirmed the presence of botulinum A toxin. She had return of a gag reflex three days after botulism immune globulin administration, with full gag reflex on the day of extubation. She remained in the hospital for a 4-week course with a total of 10 ventilator days. She was discharged with continued oromotor dysfunction requiring nasogastric tube feeding, but her neurological exam was otherwise normal.

Discussion

The symptoms of infant botulism have been well described as descending paralysis, optic palsy, decrease in symmetric facial movements, poor feeding, and weak cry followed by constipation and hypotonia.² Both of these cases involved presentations that were atypical, with altered mental status (inconsolability and somnolence) as the presenting symptom. Although altered mental status can be present in wound and food-borne botulism, it is not common in the infant form.⁷ Both patients initially presented with central neurological symptoms, and in 1 case, fever prompted initial evaluation and treatment for infection and metabolic disorders. Neither infant had been fed with anything other than infant formula or breastmilk, and neither had known outdoor exposures at time of admission. With neither infant showing the classically described symptoms of infant botulism, the diagnosis was not considered for several days even after the onset of symptoms. Patient A eventually developed a weak cry and Patient B had decreased feeding and somnolence, but neither

exhibited optic palsy, descending paralysis, or constipation in the first few days after presentation.

Infant botulism treatment includes supportive care, but the course of illness can be reduced with early treatment with botulism immune globulin. With broad initial differential diagnoses in both children with initial concerns for more common metabolic disorders or infectious disorders, the initial collection of stool samples and testing was delayed, but still within the treatment window of 7 days from the onset of symptoms with a mean of 4 days until administration.^{4,5} Treatment with botulism immune globulin (intravenous) decreases hospital length of stay from 35 days to 15 days on average.⁸ In addition, infants treated earlier in the course (within 3 days) have further reductions length of stay and long-term sequelae compared to infants treated within 4-7 days of symptom onset.⁵ The delay in administration in these cases was due to the unusual presentations.

Patient B had the additional confounder of timing with immunizations. Fever is not associated with infant botulism, and high fever of 102°F in an infant is more concerning for a serious bacterial infection or an underlying metabolic derangement. Fevers, especially high fevers, are rare with botulism and usually are due to secondary bacterial infections or wound botulism.⁷ Patient B's presentation was confounded by the timing with immunizations, which as a stressful event can precipitate metabolic derangements. Infants with underlying metabolic disorders can have metabolic crises precipitated by immunizations and often present within days of the immunizations with fevers and encephalopathy.^{9,10} Because of patient B's fevers and neurologic symptoms, metabolic disorders were considered, but with a good response to botulism immune globulin further metabolic testing, beyond that described above, was not performed.¹¹ With further progression of Patient B's course, along with no improvement after several days post immunizations and an otherwise unremarkable laboratory evaluation, administering botulism immune globulin was determined to be more beneficial than continuing supportive treatment only. The apparent dehydration seen upon admission was consistent with autonomic derangements that can be present in infants with infant botulism, such as decreased salivation.⁷ Patient B received treatment within the window and recovered.

Other conditions that can cause symptoms similar to those of infant botulism should always be considered in potential cases; in one study, spinal muscular atrophy (SMA) was identified in 19% and metabolic disorders in 16% of cases with other identified causes of negative laboratory confirmed infant botulism like illnesses.¹¹ For both infants presented here, conditions other than botulism became less likely after several days of metabolic laboratory evaluation showed normal values. Patients with SMA type 1 can present in the timeframe that the infants presented in our series, however the altered mental status of the infants does not fit with SMA.

Botulism is a reportable disease to the Centers for Disease Control and Prevention (CDC) which maintains a database of the cases that are reported from throughout the United States.¹² Although botulism can be associated with canned goods and honey in infants, there is a higher likelihood of environmental exposure if the patient's history does not support those sources. *Clostridium botulinum* is ubiquitous in the soil world-wide (except for Africa) and can be a source of disease in infants.⁶ Cases of infant botulism have been reported in all 50 states; the states with the highest annual incidence of reported cases include California, Maryland, New Jersey, Pennsylvania, and Texas.¹² In Alaska, food-borne botulism associated with home canned foods is more common than other parts of the country.¹² In Hawai'i, where both cases presented, no cases were reported to the CDC from 2008-2016, and 3 cases including these 2 were reported in the last 3 years.¹² The recent increase in cases in Hawai'i shows there is a need for awareness, better identification, and timely treatment. When evaluating infants with altered mental status, botulism should be strongly considered if other diagnoses do not fit the initial evaluation or symptomatology progresses.

Conclusion

A high index of suspicion for *Clostridium botulinum* is necessary in patients with altered mental status without a readily identifiable cause, particularly for patients who present in areas of low botulism prevalence, such as Hawai'i. Providers who are considering a diagnosis of infant botulism should make early contact with the IBTPP to help facilitate diagnosis and treatment.⁶ Careful attention to symptom progression including constipation and loss of reflexes is important in making this diagnosis in atypical cases such as those presented. Timely use of botulism immune globulin is associated with improved outcomes including decreased length of stay and time in the intensive care unit. Both patients presented here showed improvement in their reflexes and respiratory effort after the use of botulism immune globulin prior to definitive botulism diagnosis. In infants with unusual presentations, such as altered mental status and fever without other identified causes, providers should consider infant botulism.

CPT August and LTC Hamele are officers in the United States Army. The views in this article are their own and do not reflect the views of the United States Army, Department of Defense, or the United States Government.

Conflict of Interest

None of the authors identify a conflict of interest.

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