A floppy infant
Muhammad Waseem, Joel Gernsheimer, Tae K Park, Fernando Jara, Evelyn Erickson

ABSTRACT
Introduction: Infant botulism is a relatively uncommon but potentially life threatening cause of a septic appearing or lethargic infant. Case Report: A 6-week-old male infant presented to the emergency department with a history of poor feeding and fever for several days. His parents reported that he had been “more sleepy than usual” and had a weak cry. He had not passed any stool for five days. He was receiving a topical home herbal remedy for whitish lesions in his mouth. The rest of his review of systems and past medical history was non-contributory. On arrival to emergency department, he was ill appearing and lethargic. His vital signs were: temperature 101°F, heart rate 152/min, respiratory rate 44/min and oxygen saturation 99%. He had poor muscle tone and generalized weakness. He was diagnosed with infant botulism. Conclusion: It is extremely important that the diagnosis of infant botulism be suspected and appropriately treated when any infant presents with progressive weakness. Since infant botulism is a treatable condition, prompt diagnosis is therefore important in reducing morbidity and mortality.

Keywords: Infant botulism, Clostridium botulinum, Weakness

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INTRODUCTION
Infant botulism is a relatively uncommon but, potentially life threatening cause of a very ill appearing infant. We present the case of a six week old infant who presented to the emergency department (ED) with progressive neurological weakness that ultimately required ventilatory support. The differential diagnosis of weakness in the young infant is discussed and the pertinent literature is reviewed.

CASE REPORT
A 6-week-old male infant presented to the emergency department with a history of poor feeding and fever for several days. His parents reported that he had been “more sleepy than usual” and had a weak cry. He had not passed any stool for five days. He was receiving a topical home herbal remedy for whitish lesions in his mouth. The rest of his review of systems and past medical history was non-contributory.

On arrival in the emergency department, he was ill appearing and lethargic. His vital signs were: temperature 101°F, heart rate 152/min, respiratory rate...
44/min and oxygen saturation 99%. His pupils were both equally dilated but reacted to light. His tympanic membranes were normal. Examination of his pharynx was normal. No whitish lesions were seen in his mouth and it is not known what the reported whitish lesions were, although it was speculated that they could have been from candidiasis. His neck was supple. His chest was clear with good bilateral breath sounds. The cardiovascular examination was normal. His abdomen was soft and non-tender, but bowel sounds were diminished. The neurological evaluation revealed that he was lethargic with a weak suck, cry and gag reflex. He had bilateral weakness of his facial muscles. He had poor muscle tone and weakness of his extremities. The deep tendon reflexes could not be elicited. His complete blood count, serum chemistries, urinalysis, chest X-ray and head CT scan were all normal. Lumbar puncture was performed and analysis of his cerebrospinal fluid was normal.

While being monitored in the emergency department, it was noted that he had frequent episodes of oxygen desaturation and apnea. He was intubated and placed on a ventilator. The diagnosis of infant botulism was suspected and subsequently was confirmed by stool studies. *Clostridium botulinum* spores were seen in his stool and botulinum toxin was detected in samples of his stool. He was given intravenous botulism immune globulin. After receiving the immunoglobulin, this infant improved gradually over a period of three weeks. He was able to breathe on his own, and was extubated two weeks after receiving the immunoglobulin therapy. He was discharged without any evidence of residual neurological deficits three weeks after his initial presentation. Unfortunately, this patient was lost to clinic follow-up, and we were unable to contact the family to find out about the patient’s current status.

### DISCUSSION

The diagnosis of infant botulism should be strongly suspected in any infant with an acute onset of weakness in sucking, swallowing or crying, ptosis, inactivity and constipation. However, because infant botulism is an uncommon disorder it is often missed, leading to disastrous consequences.

**Pathophysiology and Epidemiology:** Botulism is a rare but potentially fatal paralytic disorder caused by a neurotoxin produced by *Clostridium botulinum*. This toxin, which is one of the most lethal poisons, causes an irreversible block of stimulation induced presynaptic cholinergic transmission. The toxin mainly affects the peripheral cholinergic nervous system. Because it does not affect adrenergic neural transmission and it does not readily cross the blood brain barrier. Botulism can be acquired in multiple ways, such as ingestion of spores that colonize the gastrointestinal tract and produce the toxin, ingestion of contaminated food that already contains the toxin such as sea food, sausages and canned foods, and infection of a wound by *Clostridium botulinum* which then produces the toxin in the wound. An important example of this is the injection of contaminated “Black Tar Heroin” [1, 2].

Infant botulism is due to colonization of the gastrointestinal tract of the infant by *Clostridium botulinum* that then produces the neurotoxin which spreads throughout the body via the circulation. Infant botulism was first recognized in 1976, and since then many cases have been reported in the United States making it the most frequently recognized form of botulism [1–3].

Infant botulism affects infants between one week and one year of age. Most cases occur within the first six months of life with a peak incidence at 3–4 months of age [3]. The majority of cases in the United States probably are caused by ingested spores that are present in dust that becomes contaminated by activities such as construction. The soil in some states such as Pennsylvania, Utah and California are particularly rich with *Clostridium botulinum*. Although cases of infant botulism from ingestion of *Clostridium botulinum* spores in raw honey or home canned foods have been reported, this is less common than previously thought [4]. It was initially postulated that the home made remedy that this baby was given may have contained raw honey or corn starch that was contaminated with *Clostridium botulinum* spores, but the parents denied that these ingredients were in this home remedy and we were unable to get a sample of it to test. It is much more likely that the infection in this infant was from *Clostridium botulinum* spores in the soil that were released into the air from local construction, and entered the baby’s gastrointestinal tract. At the time of this case, there was a lot of construction being done in the South Bronx, where this infant’s family lived. Ingestion of spores that are released into the air from soil due to construction is the most common method of infants developing botulism in the northeastern parts of the United States.

The incubation period for Botulism is thought to be at least three days. There are eight *Clostridium botulinum* toxin types. The majority of the infant botulism cases are caused by type A and B [4]. Interestingly, breast fed infants appear to be protected from botulism.

**Table 1: Important Causes of Weakness in an infant**

| Cause                               |
|-------------------------------------|
| Sepsis                              |
| Meningitis/encephalitis             |
| Hypothyroidism                      |
| Pompe disease (Glycogen storage disease type II) |
| Electrolyte disturbance             |
| Spinal muscular atrophy             |
| Neonatal myasthenia gravis          |
| Botulism                            |
| Guillain-Barré syndrome             |
| Congenital myotonic dystrophy       |
Clinical Presentation: The clinical presentation of infant botulism includes progressive neuromuscular weakness which can be mild to severe. This may be misinterpreted on examination as lethargy. Cranial nerves are affected first by the muscles of the trunk, extremities and diaphragm [4]. This may cause respiratory failure. Lethargy and poor feeding are often the initial presenting symptoms of infant botulism [1]. Constipation and weak cry are other historical features. Occasionally, a history of ingestion of raw honey or canned food may be present.

This initial presentation is followed by progressive descending weakness and hypotonia, so that the infant appears to be “floppy”. Bulbar involvement, often but not always, presents with poor sucking and gag reflexes, dilated pupils with poor response to light and accommodation, decreased eye movement, ptosis and facial paralysis. Absent deep tendon reflexes, especially with type B, toxin often occurs [5]. Occasionally, young infants may present with only a history of poor feeding followed by rapid collapse or deterioration [6].

Differential Diagnosis: The differential diagnosis of the weak and floppy infant is extensive (Table 1) and includes both neurologic and systemic diseases such as sepsis, hypothyroidism, ingestions and metabolic disorders. Because many disorders can mimic infant botulism, which is a relatively rare condition, it is often not considered initially and is then missed [6].

Sepsis is the most common diagnosis that mimics infant botulism. Most patients with infant botulism are usually afebrile. In addition, sepsis does not have cranial nerve and other neurologic findings that are often present in patients with botulism. Electrolyte disturbances, including hypoglycemia may cause lethargy and weakness.

Several disorders that cause neuromuscular weakness deserve special mention. Tick paralysis is caused by a neurotoxin secreted by a wood or dog tick that prevents liberation of acetylcholine at the neuromuscular junction. The patient usually presents with ataxia and then develops a rapidly progressive ascending flaccid paralysis that can cause respiratory failure and death. Bulbar findings, including dysphagia, dysarthria, facial paralysis and ocular muscle weakness can occur late in the course of this illness as compared to botulism where bulbar findings occur early and there is descending rather than ascending paralysis. Whenever a patient presents with rapidly progressive paralysis, tick paralysis should be suspected and a careful search should be made for the presence of a tick which should then be removed if found, and this removal often results in rapid improvement.

Guillain-Barré syndrome is another differential diagnosis. It presents as a progressive symmetrical ascending paralysis which starts in the lower extremities. Its progression is comparatively slower than tick paralysis. Cranial nerves are rarely affected, although a Miller-Fisher variant causes facial paralysis. The pupils are not affected. Lumbar puncture shows cells and high levels of protein in the CSF, whereas CSF analysis is normal in botulism.

Poliomyelitis, which is now rare but may occur in unvaccinated children, presents with high fever, meningeal signs, asymmetrical weakness and lymphocytosis in the CSF.

Myasthenia gravis is the most common disorder of the neuromuscular junction in children. It can occur as transient neonatal myasthenia gravis in infants who are born to mothers who have myasthenia or as congenital myasthenia. Infants with myasthenia have generalized weakness and hypotonia; however, deep tendon reflexes are present. Facial weakness and bulbar paralysis may often occur causing poor suck and swallowing and a weak cry. Ptosis may also be seen. Respiratory failure necessitating ventilatory support may occur. Myasthenia usually responds well to treatment with anticholinesterase inhibitors, such as neostigmine or edrophonium.

The diagnosis of infant botulism is clinical. Treatment should not be delayed pending laboratory confirmation. Although not pathognomonic and not always present early in the disease, electromyographic findings consistent with infant botulism strongly support this diagnosis in the presence of appropriate clinical setting. A clinical diagnosis is supported by the identification of C. Botulinum spores in the stools and confirmed by the identification of the toxin in the stool. Serum samples are often negative in patients with infant botulism. Our patient had both spores and toxin in his stool. Serum testing was not available at our institution. Toxin may be detected in contaminated food, if a specific food is involved.

Management: Supportive care, especially ventilatory support as needed, with very close monitoring is paramount in management of botulisms. Botulism Immune Globulin IV (BIG-IV) which is a botulinum antitoxin derived from humans is very safe and effective. It should be administered immediately in the presence of a reasonably certain clinical suspicion. Botulism Immune Globulin Intravenous (Human) (BabyBIG, USA) was administered at a dose of 50 mg/kg to our infant, which at that time was the recommended dose. It should be noted that since March of 2012, the recommended dose of BabyBIG is 75 mg/kg. BabyBIG interrupts the progression of weakness by blocking the accumulation of toxin in the nerve terminals. It reduces complications, relapses, length of intubation and hospitalization. Antibiotics have not been shown to assist in the treatment of infant botulism. In fact, in the past it was recommended that antibiotics should not be used in infant botulism because lysis of C. botulinum in the gut would release more toxins into the gut and then into the circulation. However, BIG-IV therapy destroys all of the toxins in the gut and will block absorption of toxin for at least six months. If needed antibiotics can then be safely used to treat secondary infection. Antibiotics and debridement, as needed, are definitely indicated to treat wound botulism. Penicillin or metronidazole can be used, but aminoglycosides should not be used as they worsen the effects of botulinum toxin [6]. Given the age and septic appearing presentation, many of these infants usually receive broad spectrum antibiotics.
CONCLUSION
We presented a case of an infant with botulism. It is extremely important that the diagnosis of infant botulism be suspected and appropriately treated when any infant presents with progressive weakness. Since infant botulism is a treatable condition, prompt diagnosis is very important in reducing morbidity and mortality. Early recognition allows expeditious and appropriate treatment, which saves lives.

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Author Contributions
Muhammad Waseem – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Joel Gernsheimer – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Tae K Park – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Fernando Jara – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Evelyn Erickson – Acquisition of data, Drafting the article, Final approval of the version to be published

Guarantor
The corresponding author is the guarantor of submission.

Conflict of Interest
Authors declare no conflict of interest.

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