Infant Botulism in a 2-Month-Old Female

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Abstract

We present a classic case of infant botulism in a two-month-old female treated at Children’s Hospital of Nevada at UMC. Infant botulism is a rare neuromuscular condition that results from ingestion of neurotoxins produced by the \textit{C. botulinum} bacterium. The condition was first described in California in 1976, and typically affects infants less than 12 months of age. The immature intestine of an infant is a hospitable breeding ground for the \textit{C. botulinum} bacterium to produce its potent neurotoxin. The toxin acts by blocking presynaptic cholinergic transmission and effectively inhibits the function of smooth muscle, skeletal muscle, and the autonomic nervous system. The treatment for infant botulism is BIG-IV, a human-derived antitoxin which has led to a reduction in the length of hospital stay, dependence on mechanical respiratory support, and health care cost.

Keywords: Infant Botulism; Hypotonia; Clostridium botulinum

Abbreviations

KUB: Kidney, Ureters, Bladder; TSH: Thyroid Stimulating Hormone; ICU: Intensive Care Unit; BIG-IV: Botulism Immune Globulin Intravenous

Introduction

Botulism is a potentially debilitating neuroparalytic disorder caused by the toxins produced by \textit{Clostridium botulinum} (\textit{C. botulinum}), and rarely by \textit{C. butyricum} and \textit{C. baratii}. Infant botulism occurs when infants ingest \textit{C. botulinum} spores resulting in germination, colonization, and release of toxins [1]. Although the incidence in the United States is 2 in 100,000 live births, it is essential to appropriately and quickly recognize the signs and symptoms of infant botulism as the illness can potentially lead to respiratory failure.

Case Report

We present the case of a 2-month-old previously healthy female without significant risk factors, who presented with generalized muscle weakness and poor feeding. She was born full-term at 39 weeks gestational age and had an unremarkable prenatal and postnatal course.

Ten days prior to admission, following her 2-month well child check, the patient’s parents noted progressively worsening diffuse weakness and difficulty latching during breastfeeding. In addition, the parents reported a 7-day history of constipation.

The patient was subsequently evaluated with a laboratory workup (complete blood count, complete metabolic panel, TSH, creatinine kinase, etc.), blood cultures, urine and cerebral spinal fluid, and imaging (head ultrasound, mandibular x-ray, KUB radiography, and chest x-ray) - all of which were unremarkable. The patient was stable with normal vital signs and no dysmorphic features. On physical examination, she was noted to have acute bulbar signs including poor pupillary constriction in response to light, lid lag with mild ptosis on the left, weak gag reflex, and an almost absent suck reflex. During this time, the parents were questioned thoroughly regarding exposures, contacts, and triggers. Both parents denied any ingestion of canned products, honey, or herbal supplements, and stated that the baby was breastfed and received daily vitamin D supplementation. The only notable environmental exposure reported was a recent construction project near their home.

Given the examination findings and history, infant botulism was suspected. Precautions to monitor for and respond to respiratory failure were established. The pediatric infectious disease, neurology, and ICU teams were notified. Stool testing for botulinum toxin was sent and the result was positive for botulism toxin A, however, due to the high index of suspicion treatment was started prior to receiving...
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The patient showed marked clinical improvement over several days after administration of BIG-IV and the infant's strength and tone steadily improved. The patient was managed with supportive care and close monitoring, however, escalation of care such as intubation or transfer to the pediatric ICU was not required. As the clinical picture continued to improve, speech therapy was consulted and noted a steady improvement in the infant’s suck reflex and ability to tolerate feeds by mouth. The patient was discharged 12 days following admission to her neurologic baseline.

Discussion

Important diagnoses to consider when evaluating an infant with hypotonia and weakness include 1) metabolic disease, 2) genetic conditions such as spinal muscular atrophy or muscular dystrophy, 3) endocrine malfunction such as hypothyroidism, 4) infections such as infant botulism and 5) drug ingestion/toxicity.

Relevant workup includes general blood testing with complete blood count, electrolytes, liver function tests, thyroid testing, creatinine kinase, urine organic acids, serum amino acids, serum ammonia, lumbar puncture, and potential head/neck imaging if concerned for neurologic origin of symptoms. In our patient, all of these tests were sent at various stages of evaluation to rule out other causes of hypotonia and weakness, which further increased our suspicion of infant botulism as each test came back negative.

Infant botulism, first identified in California in 1976, affects infants between one week and twelve months of age. It is the most common clinical form of botulism in the United States with between 70 and 100 cases recognized annually. The immature intestine of an infant is a hospitable breeding ground for the C. botulinum bacterium to germinate, multiply, and produce its potent botulinum neurotoxin [2]. This hypothesis is supported by animal studies demonstrating that infant mice experience age-related susceptibility to botulism colonization of the gastrointestinal tract [3]. Although infant botulism is a rare diagnosis it remains imperative that clinicians include it in the differential for an infant who presents with bulbar dysfunction, weakness, and/or respiratory failure. This is especially true in endemic areas and environments that favor persistence of the spores in the soil.

The case of our 2-month-old at Children’s Hospital of Nevada at UMC exhibits a classic clinical presentation of infant botulism. This condition and its clinical picture can be frightening for parents and clinicians alike. Fortunately, our understanding of infant botulism has drastically evolved since its identification in 1976. This evolution is in part thanks to whole genome sequencing which has shed considerable light on the biology, neurotoxins, and medical management of infant botulism [2-5]. The C. botulinum bacterium is composed of four different sub-groups, I through IV, which altogether make seven botulinum neurotoxins, type A through G. Neurotoxins A and B are responsible for the majority of infant botulism cases and type A (isolated from our patient) is more prevalent in the western United States. The neurotoxins act by irreversibly binding cholinergic receptors in the presynaptic cell membrane of voluntary motor and autonomic neuromuscular junctions. This causes failed neuromuscular transmission and thereby inhibits the function of skeletal muscle, smooth muscle, and the autonomic system. Botulism is the deadleat poison known to humans with a lethal dose of only $10^{-9}$ mg/kg of body weight. The hypothesized incubation period ranges from 3 to 30 days [3].

This case set in motion clinical practice guidelines which will guide management of future infant botulism cases in Las Vegas. The Nevada Department of Health and Human Services will play a critical role in ensuring the safety of over-the-counter and nutritional infant products. The Health Department collected samples in an effort to isolate C. botulinum from the patient’s infant formula and ZarBee’s Baby Gripe Water (a product containing agar). We suspect that the spores were harbored in dust particulate from a neighboring construction site, however, environmental testing was never performed. The search for a source was guided by previous reports which have shown honey, soil and dust to be the top offenders that harbor C. botulinum spores. Other documented sources include powdered infant formula, infant cereal, natural sweeteners, and corn syrup [6-8]. The isolation of C. botulinum from one of these products would present a serious and novel food regulation problem. A single case of infant botulism can signal a national emergency, therefore laboratory tests for C. botulinum organisms and toxins are highly specialized and suspect samples must be sent urgently to the local Health Department and the Center for Disease Control.

This case also represents the importance of early identification based on clinical skills rather than diagnostic testing in the treatment of infant botulism. Although the incidence in the United States is rare, the disease itself can lead to life-threatening complications. Seventy percent or more of infants with botulism will require intensive care for mechanical ventilation, and the average hospital stay is about 44 days. A major advantage of BIG-IV is that it has been shown to reduce the mean length of hospital stays by three weeks [5,6]. It also decreases the amount of time that patients spend in ICU, that patients require mechanical respiratory support, and that patients receive tube feeding or TPN. The latest estimates also posit that BIG-IV reduces hospital charges by $90,000 per patient. The treatment is beneficial for both type A and type B neurotoxins and is not associated with any serious adverse side effects. Strong clinical diagnostic skills can

allow for timely treatment of infant botulism and reduce mean hospital stays from 4 - 6 weeks to about 2 weeks, as well as minimize any hospital-acquired complications [5-7].

Conclusions

Lessons for the clinician to take from this case report include:

1. While infant botulism is a rare diagnosis, it remains imperative that clinicians include it in the differential for an infant who presents with bulbar dysfunction, weakness, and/or respiratory failure.

2. Early identification is based on clinical skills rather than diagnostic testing, and it is imperative to start treatment immediately if there is high clinical suspicion of infant botulism.

3. Rapid identification of infant botulism cases is important as BIG-IV treatment has been shown to reduce the mean length of hospital stays by three weeks and to cut healthcare cost by $90,000 per case.

Conflict of Interest

No conflict of interest to declare.

Bibliography


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