Infant Botulism — Diagnosis and Treatment

Botulism is a neuromuscular paralysis secondary to a neurotoxin secreted from Clostridium Botulinum bacteria. It is a rare syndrome that results from food poisoning with the spore-forming Clostridium bacteria. The ingested food is contaminated with the pre-secreted botulinum toxin. Infant botulism occurs with the ingestion of the Clostridia spores that later germinate and colonize the intestine and secrete the neurotoxin. Other forms of botulism include wound botulism, where the toxin is secreted in infected wounds, inhalational botulism in biological wars, and iatrogenic botulism which occurs rarely in people using botulinum toxin for cosmetic purposes.

Introduction

Botulism is a disease of neuromuscular paralysis, secondary to a neurotoxin secreted from Clostridium Botulinum bacteria. Infant botulism is the most common form of botulism worldwide. Other forms of botulism that affect older age groups include:

- Wound botulism, which is common among the military. Inoculation of the spores deep in the tissues presents a good environment for germination and toxin secretion. Polymicrobial bacterial infection can be present in wound
botulism. Wound debridement, antitoxin therapy, antibiotics and tetanus toxoid are recommended for management.

- Foodborne botulism that occurs after eating home canned foods that contain bacterial toxins.

Epidemiology

It is more common between the second and eight months, but it can also happen any time up to the first year of life. It is a rare disease that affects up to 100 children annually in the United States.

Etiology & Risk factors

The disease arises from **neurotoxin secreted from Clostridium Botulinum bacteria that is acquired through various mechanisms such as**:

1. Ingestion of honey. Honey is a source of bacterial spores that germinate in the infant’s alimentary tract and start producing the neurotoxin in vivo.
2. Ingestion of dust containing toxin-producing bacteria spores.
3. The introduction of milk formula and solid foods increase infants’ vulnerability to the bacteria.

Microbiology of Botulism

*Clostridium Botulinum* is a group of gram-positive anaerobic bacilli which are able to form spores during unfavorable environmental conditions. The spores are heat resistant for up to 100 ºC for hours and hence they can be easily transmitted via food. With low acidity, oxygen and appropriate temperature; the spores germinate into the toxin-producing bacteria.

The bacteria is commonly isolated from the soil and can be found on the surfaces of vegetables and fruits. The toxin produced by *Clostridium botulinum* is the most potent known toxin with the least known minimal lethal dose. It is a heat labile protein that can be easily denatured by temperatures above 80 ºC. However, it can resist the gastric acidity and proteolytic enzymes of the gut. It is easily absorbed through the stomach or the intestinal mucosa to the bloodstream.

The Botulinum toxin affects the presynaptic cholinergic transmission of sensory, motor and autonomic nerve fibers leading to neuromuscular paralysis. The toxin reaches the central nervous system through systemic spread or axonal transport and can inhibit the release of dopamine, serotonin, somatostatin, gamma-aminobutyric acid and noradrenaline from presynaptic neurons.
Clinical Picture of Botulism

The disease has an incubation period of between 3-30 days after which the patients present with **symmetric descending weakness** with **bilateral cranial neuropathies without fever or mental dysfunction**. The weakness of muscles supplied by cranial nerves followed by weakness of the limbs and diaphragm are characteristic.

Some cases have gastrointestinal symptoms as the most predominant symptoms. In infants less than 12 months old, colonization of the intestine with *Clostridium Botulinum* bacteria present early with **constipation** which may be the first sign. This is followed by progressive **hypotonia and loss of deep tendon reflexes**. Cranial neuropathies present with a **weak cry, poor sucking and feeding, drooling, ptosis and pupillary paralysis**. Autonomic dysfunction may be present with **dry mouth, dry eye, fluctuating heart rate and blood pressure**.

Ingestion of the preformed toxin in foodborne botulism presents first after few hours with:

- nausea, vomiting, diarrhea, dry mouth and pain
- symmetric descending weakness of the trunk and limbs
- Blurring of vision, diplopia and ptosis are neurological manifestations due to the involvement of the cranial nerves III, IV and VI
- Other cranial nerve involvement leads to dysarthria, dysphagia and facial palsy
- Diaphragmatic paralysis is common, and patients eventually need intubation and mechanical ventilation
- Urine retention is also common and results from smooth muscle paralysis

Differential Diagnosis of Botulism

Other forms of neuromuscular paralysis include Guillain-Barré syndrome, tick paralysis, myasthenia gravis, poliomyelitis, antibiotic-associated paralysis and Lambert-Eaton myasthenic syndrome.

Infant botulism should be differentiated from metabolic encephalopathy, brainstem encephalitis, sepsis, spinal muscular atrophy type 1, neonatal myasthenia gravis and dehydration.

Diagnosis of Botulism

Clinical suspicion is important as early administration of antitoxin therapy is lifesaving while waiting for culture results and confirmatory tests. Detection of the botulinum toxin in the serum of suspected individuals is diagnostic.

The toxin can also be isolated in the stool, vomit or food remnants of the suspected individuals. Repetitive nerve stimulation and electromyography can be used to differentiate between myasthenia gravis, LEMS and botulism—especially wound botulism. CSF is usually normal.

Infant botulism: the spores and the toxin can be isolated from the stool of infected infants but not in the serum. The diagnosis usually takes a few days until the results of the culture are positive or the toxin is detected in stool samples.
Management of Botulism

Patients with suspected botulism should be monitored closely in the hospital or even the ICU to ensure adequate respiration and oxygenation. Many patients will need intubation and mechanical ventilation to prevent respiratory failure and airway compromise. Adequate feeding should be continued for prolonged respiratory support with a nasogastric tube or even parenteral nutrition.

Antitoxin therapy should be administered to all patients based on clinical suspicion of botulism without waiting for confirmatory tests. It is proven to decrease mortality rates for patients diagnosed with botulism even with a long period of symptoms. Patients presenting with a febrile descending paralysis and cranial neuropathies should be evaluated for botulism.

There are two types of antitoxin therapy: equine serum heptavalent botulism antitoxin and human-derived botulism immunoglobulin. The equine serum heptavalent botulism antitoxin includes antibodies against 7 types of botulin toxins. It is mainly administered for adults and children older than one year. Hypersensitivity reaction with anaphylaxis and serum sickness can result from the equine serum antitoxin; thus skin test, desensitization, and proper dosing are important prior to therapy. Other adverse effects include rash, nausea, fever, headache, and chills.

Human-derived botulinum immunoglobulin is used for infants less than 12 months of age.

Antibiotics can be given for patients with wound botulism due to infection, but they are contraindicated in patients with infant botulism or foodborne botulism. Antibiotic-mediated lysis of the Clostridium bacteria can increase the toxin amount and its absorption in the circulation.

Prevention of Botulism

Prevention of foodborne botulism depends mainly on proper canning of food. Boiling of food before consumption is sufficient to denature the heat labile toxin. For infant botulism, prevention is mainly achieved with avoidance of honey in infants less than one-year-old. Early treatment is mandatory in infants with no history of honey consumption.

Avoidance of exposure to dust in areas that have high toxin content in the soil has been shown to reduce the occurrence of the disease.

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