Zach's Ruff Two Weeks

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Introduction

Botulism is a lower motor neuron, paralytic illness that is caused by intoxication with a neurotoxin produced by the bacterium *Clostridium botulinum*. This is a gram positive, motile, spore-forming, anaerobic rod-shaped bacteria that is dispersed within the soil worldwide. It can also be found in uncooked food, carrion, and within improperly stored silage or other plant material. Spores form when the bacterium finds itself in an inhospitable environment. The spores are robust as they can be resistant to heat, light, desiccation, chemicals, and radiation. Once ingested, the spores germinate in the intestinal tract and colonize with the neurotoxigenic clostridia. Fortunately, occurrence is sporadic and rare. Dogs are almost always affected with *Clostridium botulinum* neurotoxin serotype C. This neurotoxin interferes with the release of acetylcholine at the neuromuscular junction which in turn results in diffuse lower motor neuron signs.[1]

There are seven types of *C. botulinum* that have been identified and are individually distinguished by their antigenically distinct types of botulinum neurotoxin that they will produce. Each of these types (A, B, C, D, E, F, and G) are similar in structure and each have the same neurotoxic effect. Types C and D are the two types that cause disease in birds and in other mammals.[2] All canine cases have be caused by type C toxin, with an exception of two cases reported in Senegal that had type D. Cats are typically not naturally affected and illness has only been induced experimentally.[4]

Most patients affected with botulism will present with hyporeflexia and hypotonia, indicating a lower motor neuron disease. These clinical signs could be associated with several differentials including tick bite paralysis, myasthenia gravis, acute canine polyradiculoneuritis (coonhound paralysis), rabies, and less likely coral snake venom toxicity.[1]

History and Presentation

Zach, a 3 year old, neutered male, mixed breed dog weighing 11.6 kgs was referred to the Mississippi State University College of Veterinary Medicine Neurology service on 10/8/18 for evaluation of a 24-36 hour history of rapidly progressing, ascending flaccid tetraparesis. On the previous day, 10/7/18, Zach's owners noticed him acutely down in their back yard. He was unable to stand and use his back legs, but his forelimbs were still functional at that time. He was taken to the Mississippi State University Animal Emergency and Referral Center (AERC) in Flowood, MS where anamnesis was taken and a physical examination performed. Complete blood count (CBC), serum chemistry profile, and radiographs were performed. His clinical pathology results revealed a slight neutrophilia at (16.14 K/uL, reference: 2.95-11.64 K/uL) and radiographs were unremarkable. He was thoroughly searched for ticks with none being found. Credelio chewable (lotilaner) was administered orally, in case his signs were due to tick paralysis. Lotilaner was chosen for its rapid action against ticks with expected activity within 4 hours. Overnight, Zach did not show improvement and was referred to the Mississippi State University Veterinary Specialty Center (VSC) the following morning for further evaluation and care. Further questions for Zach's owners revealed an old pot roast had been discarded nearby, and they were fairly certain that Zach had eaten some or all of it. On presentation to the VSC, Zach was quiet, but alert and responsive. Physical examination revealed a mildly elevated heart rate of 164 beats per minute and respiratory rate of 64 breaths per minute. His temperature was normal (100.5F.) Otherwise, his physical examination was unremarkable and another thorough search for ticks was negative. Neurological examination revealed normal cranial nerves initially. He was non-ambulatory, tetraparetic with minimal motor function in all 4 limbs but a strong tail wag. Postural reactions were absent in all 4 limbs (suspected to be due to profound lower motor

neuron weakness.) Muscle tone was markedly reduced in all 4 limbs. His biceps reflexes and cranial tibial reflexes were intact bilaterally, however all other spinal reflexes were markedly reduced to absent. No pain was elicited on spinal or paraspinal palpation. Neuroanatomic localization was the neuromuscular junction. Differential diagnoses included an infectious or inflammatory disease.

Diagnostic Approach/Considerations

Upon presentation to the neurology service, his neurological exam was unchanged from presentation thus several diagnostics were performed. A creatine kinase level and an ISTAT were performed with both found to be within normal limits. With *C. botulinum* being uppermost on our list of differential diagnoses due the history and clinical signs, a fresh fecal sample was collected and sent to the University of Pennsylvania for a botulism PCR assay to test for types A, B, and C toxin. After a turnaround time of 5 days, the qualitative results were positive for *C. botulinum* Type C toxin.

Other supportive diagnostics that were not performed in this case include electromyography (EMG) and motor nerve conduction (MNC). This is a procedure that can be used to assess and record electrical muscle and nerve activity. Patients that are affected with a lower motor dysfunction, as those with botulism, will have a subnormal motor unit potential when a motor nerve is stimulated.[1]

Pathophysiology

Botulism is an intoxication caused by a toxin, produced by *Clostridium botulinum*. There are a total of seven distinct toxin types (A, B, C, D, E, F, G) that are known.

The majority of cases have occurred after ingestion of the toxin from carrion or uncooked meat. Once ingested, the toxin withstands the effects of gastric acid and is absorbed once it passes into the small intestine.[2] The toxin enters the lymphatic system by means of endocytosis and then enters the bloodstream. There, the toxin affects all neuromuscular junctions with signs of flaccid paralysis ascending from the hind limbs cranially. Additionally, the toxin binds to presynaptic cholinergic autonomic synapses, resulting in dysfunction with the autonomic nervous system. Clinical signs may include mydriasis, alterations in heart rate, urinary retention, constipation, megaesophagus, or keratoconjunctivitis sicca (KCS). The toxin binds to the presynaptic membrane of the neuromuscular junction, preventing the release of acetylcholine. The toxin is composed of a light chain and a heavy chain carboxy-terminals. The light chain is the active element of the toxin and responsible for inactivating the SNARE (soluble N-ethylmaleimide sensitive factor attachment protein receptor) found in the neuromuscular junction. These SNARE proteins control the release and fusion of the neurotransmitter vesicles which oversee the neurotransmitter release into the synaptic cleft. Toxin binding occurs rapidly and is irreversible. The toxin binds to the presynaptic endings of cranial nerves and throughout the peripheral nervous system. The lifespan of the toxin can be lengthy, only fully degraded and inactive when the last light chain molecule of the toxin is broken down.[3] The botulinal toxins only cause temporary paralysis and degeneration to the synapse. The prognosis for botulism is fair to good depending on the severity of clinical signs. Mortality is due to respiratory paralysis or complications from aspiration pneumonia. Patients usually recover in one to three weeks with supportive care provided there is significant emphasis on respiratory and nutritional support. Dogs that survive are expected to have a complete return to normal neurological function.[1]

Treatment and Management

There is no specific treatment for *C. Botulinum* Type C; supportive care is the mainstay of treatment in dogs, although if type C antitoxin is available, it can be administered intramuscularly within days of exposure. This antitoxin will bind and then inactivate toxin that is circulating that has not infiltrated the nerve endings.[2]

After being admitted, Zach was started on Lactated Ringers for dehydration as well as maropitant to mitigate nausea. He was given a dose of methadone for analgesia. One day after admission to the hospital, repeat neurological evaluation revealed that he had developed anisocoria, bilateral facial weakness, a decreased gag reflex, and a decreased menace response OU. By the next day, Zach's gag reflex and muscle tone improved along with his anisocoria. Three days after presentation, his gag reflex was normal and he was able to hold himself in a sternal position with ease. Due to his bilateral facial weakness, his eyes were stained with flourescein to check for corneal ulcers. Pinpoint corneal ulcers were present bilaterally. He was started on artificial tears, triple antibiotic ointment, and Tylenol 4 for pain associated with the corneal ulcers. Five days after presentation, Zach's spinal reflexes were noted to be improved. He began eating and drinking with assistance; though, he continued to have a waxing and waning appetite. Capromorelin, an appetite stimulant, was initiated. Within a day, Zach started eating. Two days later, his menace responses and palpebral reflexes were improved bilaterally and considered almost normal. Nine days after presentation, he was able to right himself and held himself up for about 20 seconds with assistance. Zach’s corneal ulcers were resolved. However, a Schirmer tear test indicated inadequate tear production OU. Optimmune (cyclosporine) and I-drops, (lubricant) were prescribed for the bilateral keratoconjunctivitis sicca (KCS). Twelve days

after initial presentation, Zach was able rise on his own and walk outside, where he urinated and defecated normally.

Case Outcome

Zach was hospitalized for two weeks, during which time he regained urinary continence as well as stability and ambulation (within 9 days.) Eleven days after being hospitalized in Mississippi State Intensive Care Unit, Zach was transferred to the hospital wards and then discharged three days later. Zach was sent home with cyclosporine 1% ophthalmic ointment BID OU and eye lubricants QID OU for treatment of KCS with instructions to return for a recheck with our ophthalmology department. Zach did not return for a recheck, but after following up with his owners five months later, they reported his KSC had resolved. Further, the owners report Zach demonstrates no neurologic deficits after his *Clostridium botulinum* intoxication and appears to be healthy and happy at home.

References:

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