Tongue-Tied

A Case Report of Equine Botulism

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Introduction

Botulism is a neurologic disease mainly caused by *Clostridium botulinum* and the neurotoxins that it produces. It can affect most warm-blooded animals, and horses are one of the most susceptible species[1,2,6-8]. In adult horses, the most common route of transmission is through the ingestion of preformed toxins in contaminated feed material. The incubation rate after ingestion is variable and thought to depend on the amount of toxin ingested[7,8]. Horses typically present with generalized weakness that may progress to full recumbency. Other common signs include dysphagia, decreased tongue tone, decreased tail tone, and delayed pupillary light and palpebral reflexes[1-3,6,7]. Death typically occurs due to respiratory failure. Treatment includes prompt administration of botulism antitoxin and supportive care[2,7]. Even when treated, there is only a 48% survival rate for adult horses. However, horses that retain their ability to stand throughout treatment have a much-improved prognosis with a survival rate of 95%[3].

History and Presentation

Ermac, an approximately 5-year-old Paint Horse gelding, was presented to MSU-CVM Equine Department on March 27, 2019 for possible choke. He is housed on 2 acres with another horse and a donkey. He has grazing available and is also fed grain and Bermuda grass hay. The owners reported that they switched to square bales after noting that the round bale looked of poor quality and moldy. On March 23rd they saw Ermac eating from the remains of that round bale. On March 25th, the owners noted that Ermac was becoming lethargic and quieter. On March 26th they started noticing that Ermac was dropping his feed, but he still had a good appetite and was drinking water. On March 27th, he became inappetent and appeared to have lost weight. He also had dark brown to black nasal discharge, was lying down frequently, and had labored breathing. Ermac was taken to his primary veterinarian where nasogastric (NG) intubation was attempted to

relieve a presumed esophageal obstruction. The veterinarian was unsuccessful in passing the NG tube, thus, Ermac was administered, flunixin meglumine, ceftiofur crystalline free acid, and referred to MSU-CVM.

On presentation, March 27th, Ermac was depressed. His heart rate was mildly elevated at 52 beats per minute, but no murmurs or arrhythmias were auscultated. His respiratory rate was 16 breaths per minute with no crackles or wheezes auscultated. His temperature was 98.8 degrees Fahrenheit. His mucous membranes were pale pink with a capillary refill time of 2 seconds. He had bilateral, mucopurulent nasal discharge. Borborygmi was decreased in all four quadrants. Ermac had a low head carriage, and when his tongue was distracted from the side of his mouth, he was not able to retract it back within the oral cavity. No other abnormalities of cranial nerves were observed at this time. He was ataxic and tetraparetic. When walking, he was able to be pulled off course in either direction by pulling on his tail. He also had poor tail tone and bilaterally, symmetrical atrophy of the epaxial and gluteal muscles. Due to his history and clinical signs, Ermac was presumptively diagnosed with botulism.

Pathophysiology

Botulism is a neuroparalytic disease that can affect many mammals, birds, and fish, with horses being one of the most susceptible species of mammals. It is caused by botulinum neurotoxins (BoNTs) that are produced by gram-positive, spore forming, rod shaped Clostridia mainly *Clostridium botulinum*, but *C. argentinense, C. baratii,* and *C. butyricum* can also produce BoNTs[1,7,8]. These clostridia produce seven serotypically distinct BoNTs, type A-G[8]. Clostridia are found in the environment worldwide, and when in spore form, they are relatively resistant to physical and chemical factors. Although found worldwide, the BoNTs are not equally distributed. In equines in the United States, toxins A, B, and C have all been reported[2,8]. Toxins

A and B are associated with the ingestion of preformed toxin due to spoilage of feedstuffs. Type B is more common accounting for 85% of cases in the US[7]. Type A is mostly in the Western US while type B is reported more often in the mid-Atlantic states and Kentucky. Type C is associated with feed contaminated by carrion[7]. BoNT producing clostridia can live in the gastrointestinal (GI) tract, usually in the spore form, of some animals. When those animals die, it allows the clostridia to vegetate and produce the toxins which contaminate the feed[2,7,8].

Once the toxin is introduced into the body (in horses, usually through the GI system) it gets into the circulation or into the lymphatics and then the circulatory system. Once in the blood, the toxins travel to peripheral nerves particularly skeletal and cholinergic nerve terminals[7,8]. Once there, they bind to proteins on the surface of the presynaptic nerve terminal in a dual receptor binding method. They first bind to polysialoganglioside on the outer surface and then a protein on the inner surface of the exocytosed synaptic vesicle. The protein that is bound differs depending on the BoNT type[8]. The vesicle is then endocytosed into the presynaptic nerve terminal. The toxin releases its L chain, which codes for a metalloprotease, into the cytosol. The metalloprotease will cleave one of the soluble N-ethylmaleimide-sensitive factor attachment protein receptor (SNARE) proteins depending on the type of toxin involved[8]. BoNT B will cleave the vesicle associated membrane protein. The SNARE proteins are associated with the exocytosis of the neurotransmitter from the presynaptic nerve[8]. The proteins that the toxins target will stop the exocytosis of the neurotransmitter (acetylcholine) in these junctions and result in neuroparalysis. The toxins do not kill the cells, making them able to recover once the metalloprotease has been broken down and new proteins formed[7,8].

Clinical signs can be seen within hours to days after ingestion and include generalized weakness and loss of muscle strength to flaccid paralysis. Horses may present with dysphagia

that can be confused with “choke”, or they appear colicky[1-3,6,7]. On initial physical exam, close attention should be paid to cranial nerves and a neurologic exam as this can give a picture of the classical botulism horse. Along with generalized weakness, they typically have decreased tongue tone, difficulty prehending feed, decreased tail tone, a base narrow stance, and decreased palpebral and pupillary light reflexes[1-3,6,7]. If not caught and treated early, the horses may progress to full recumbency and an inability to stand[1-3,7]. Death often occurs due to respiratory failure. The progression of the disease is variable as is the incubation time, although the amount of toxin ingested and the horse’s activity level may play a role[7,8].

The diagnosis of botulism is typically a clinical one. Clinical signs as described above and a history of eating spoiled feed, or a bad bale of hay should put botulism at the top of the differential list[2,7]. Other tests such as the tongue stress test and grain test can also be performed to help support a diagnosis of botulism by highlighting stereotypical clinical signs. In the tongue stress test, the tongue is withdrawn and the horse’s ability to replace it is assessed (normal is 1-2 attempts). The grain test is performed by placing 8 oz of feed in a flat pan and timing how long it takes the horse to eat (normal is less than 2 minutes). If these are prolonged, botulism is highly suspected[2]. BoNTs typically do not skew the bloodwork, but it may reflect dehydration or increased muscle enzymes if they have been recumbent for prolonged periods[7]. Specific testing for BoNT can be done from the serum, GI contents, or clostridium infected wound. Spores can be found in the feed or GI contents. The horse can also be tested for an antibody response[1,2,7]. The gold standard for testing is the mouse bioassay. This involves inoculating multiple mice with a sample or culture-enriched sample from the suspect horse and observing their response. Clinical signs in the mice indicate the presence of BoNTs[4,5,7]. The specificity for this technique is high (97%), but the sensitivity is very low (32%)[4]. Recent research has evaluated quantitative

real-time PCR for the diagnosis of botulism in horses with positive results showing similar specificities and improved sensitivities. It also allows for quicker results than the mouse bioassay. However, this technique is not yet widely used[5]. For many equine cases of botulism in practice, diagnosis is based on the clinical signs, history, and ruling out other possible disease processes. Some differentials to note are equine protozoal myeloencephalitis (EPM), equine motor neuron disease, equine herpes virus type 1, West Nile virus, rabies, and other toxin ingestions[1,7].

The mainstays of treatment for botulism include antitoxin and supportive care. Antitoxin comes either as a polyvalent mixture with type A, B, and C antitoxins, or a product containing mostly type B antitoxin[2]. The antitoxin only works on circulating toxins and will not bind to ones that have already entered a cell. Therefore, it can only stop the progression of disease; it cannot reverse any damage that has already occurred. It is imperative that this therapy be instituted as soon as possible[1,2,7]. The other facet of treatment is supportive care and managing any complications that occur. In horses with dysphagia, NG feeding tubes can be used for nutritional supplementation and hydration until they are able to eat again. They should be kept on soft bedding to decrease decubital ulcers and sores that can occur from prolonged recumbency. If fully recumbent, a sling can be used[3,7]. In dysphagic horses, aspiration pneumonia is a common complication. However, with proper management of pneumonia and any other complications, there is no detrimental effect to their survival rate[3].

Diagnostic Approach

Initial diagnostics at presentation included an abdominal and thoracic ultrasound; endoscopy of the esophagus, guttural pouches, and stomach; a venous blood gas; complete blood count; and a serum chemistry. The thoracic ultrasound revealed no abnormal findings. The

abdominal ultrasound revealed decreased GI motility. The endoscopy showed no esophageal blockage, but it did reveal a dorsal displacement of the soft palate, gastritis, and gastric bots. Ermac's bloodwork revealed a stress leukogram, moderate hypernatremia, moderate hyperchloremia, mild hyperglycemia, mild hypomagnesemia, and mildly elevated ALP, total protein, globulins, and total bilirubin. The abnormalities were thought to mostly be from dehydration and inappetence. Samples were not sent out for botulism testing because treatment needs to be started as soon as possible in suspect botulism cases, it takes a few days to weeks to get results back, and the sensitivity is so low that a negative result would not change the treatment plan.

Treatment and Management

After choke was ruled out, treatments were started for the top differentials: botulism and EPM. Rabies and West Nile virus were considered very unlikely because Ermac had been properly vaccinated for both. An 18 French NG feeding tube and a jugular intravenous catheter were placed. Ermac was given two units of trivalent antibotulism plasma with no adverse reactions noted. He was started on oral fluids, Ponazuril, Elevate WS (vitamin E supplement), ranitidine, sucralfate, Karo syrup, and flunixin meglumine. Every 6 hours, Ermac was given electrolyte fluids. Throughout that first night he was noted to be lying down in sternal recumbency for approximately half of the night. He had difficulty rising, and over the next few days he would also develop difficulty in controlling his descents.

On March 28th, Ermac was noted to have muscle fasciculations over many regions of his body such as his pectorals, gluteals, and quadriceps muscles and a low head carriage while standing. He continued to lie down as much as he was standing. He showed increased effort to stand, and he would often slide down the wall for support when lying down. Between his

continued recumbency and difficulty controlling his descents, he developed abrasions, decubital ulcers, and a seroma. The decubital ulcers developed on his hocks, fetlocks, pasterns, hips, and elbows. He had a few small abrasions around his left eye. He developed a seroma along his sternum. Leg wraps were placed on all four limbs to try to decrease trauma as he was standing and lying down. Also, on his first day hospitalized, Ermac did not urinate. His oral fluid rate was increased to try to stimulate more urine production. He did urinate the second night and continued to have normal urinations throughout the rest of his hospitalization.

On March 29th another serum chemistry was performed, and Ermac was mildly hyponatremic and moderately hypochloremic. He also had an elevated creatinine. Because of this, his fluids were increased, and electrolyte fluids were given more frequently. At this time, Ermac was started on Well-Gel. This is a complete nutritional supplement that can be made into a slurry and administered through a feeding tube. A serum sample was sent out for EPM titers. On the 30th, a large animal renal profile was performed. The creatinine had decreased to almost within normal limits. The chloride had increased, but the sodium had slightly decreased.

On March 31st, as Ermac was receiving one of Well-Gel feedings, a small amount of green, nasal discharge was noted. The Well-Gel was stopped, and the placement of the tube was assessed. It did not appear out of place at that time, and his fluids were restarted. When he was checked again, he had white frothy discharge from his nostrils bilaterally. The fluids were stopped, and his feeding tube was assessed using endoscopy. It had become kinked with a 180 degree turn that allowed the end to come back up into his nostril. A new feeding tube was placed, but throughout the next day, it continued to back out, and become difficult for medications or fluids to be administered. The feeding tube was removed and replaced with a small-bore NG tube.

During Ermac's physical exam on April 2nd it was noted that he was trying to use his tongue. His tongue was distracted from the side of his mouth and he was able to replace it. He was also seen to be swallowing at this time and was able to lift his head level with his shoulder for short amounts of time. Before this he could not lift his head. He had also started standing for longer periods of time.

The NG tube was left in place to allow the muscles involved with swallowing more time to recover. However, the NG tube came out on its own overnight on April 3rd. Ermac was offered a mash of Well-Gel and water on the 4th. He seemed to have difficulty prehending the mash from the bucket, but he was able to eat small amounts if hand fed. Since he was able to eat on his own without any nasal discharge, the NG tube was not replaced. He was also offered a senior mash and alfalfa leaves. He would cough occasionally while eating, although no discharge was noted with the cough. Ermac did well throughout that day, but overnight he developed a fever of over 102 degrees. He was started on trimethoprim sulfadiazine (TMS), and his temperature was within normal limits by the next morning.

The titers for EPM came back as 640. According to the UC Davis laboratory, titers this high have a 95% chance of contributing to the clinical signs being seen. It was decided to continue Ermac on his therapy for EPM. Even though the titers came back as elevated, botulism was still considered his main diagnosis, with EPM possibly contributing to some of his neurological signs.

On April 5th, Ermac was noted to have an increased respiratory rate and effort with moderate nostril flaring. Aspiration pneumonia was a concern due to the problems encountered with his feeding tubes and dysphagia. A rebreathing exam was performed, and normal bronchovesicular sounds were heard in all lung fields. No crackles or wheezes were auscultated.

His respiratory rate and effort continued to be closely monitored, and in a few days, they were within normal ranges.

The ulcer over his left hip had developed cellulitis and started to drain caseous material from circular wounds on April 6th. The wounds were explored with a red rubber catheter, and one had a ventral pocket. This area was lavaged with dilute iodine. Silver sulfadiazine (SSD) cream was placed on all the decubital ulcers. Prior to this, triple antibiotic ointment had been used. The pocket continued to fill with caseous material, so a ventral drainage site was made on the 9th. The next day, the pocket had started to close, and less drainage was noted. The other decubital ulcers resolved without further incident.

Ermac continued to eat well after having his NG tube removed. On April 8th, he was switched from alfalfa leaves to alfalfa pellets soaked in water. The amount fed was gradually increased and periodically he was challenged with firmer feeds and grazing. He was able to graze by April 9th, but he was not able to eat dry grain or hay by the time he was discharged. His ranitidine and sucralfate were discontinued on the 15th.

After Ermac's tongue tone started coming back, his neurologic status continued to slowly improve. He was able to hold his head higher every day and was able to stay standing for longer amounts of time. On April 15th, a neurologic exam was repeated. Ermac had improved from a grade 4/5 to a grade 2/5. His hindlimbs appeared to be weaker than his forelimbs. The left was worse than the right based on more consistent pivoting when circling left and the ability to tail pull easier to the left. He also stood base narrow, indicating postural muscle weakness. Ermac also demonstrated poor/hesitant hoof placement and variable stride length when walking up and down inclines as well as when asked to walk over planks. He was also noted to still have weakened tail tone.

Case Outcome

On April 20th, Ermac was discharged with instructions to continue his feeding regime of mashes and short times of hand grazing. He was also to be kept in a stall or small paddock for the next 6 weeks as he regained his strength. He could be hand walked 3-4 times a day. His medications of TMS, Ponazuril, and Elevate WS were continued (total of approximately 20 days on TMS and approximately 28 days on Ponazuril and Elevate). His decubital ulcers had been improving, but still had scabs, so the owners were instructed to keep these clean and to apply a thin layer of SSD cream to each of the areas. Ways to prevent botulism were discussed with his owners. In horses, botulism is not fully preventable, but there is a vaccine for BoNT type B on the market[1,7]. One study did show that horses who had been fully vaccinated were still able to acquire the disease, but they had less severe signs than other horses[3]. The vaccine is not cross protective against other toxin types. Other ways to aid in prevention include feeding good quality feeds that have been properly stored and feeding square bales instead of round bales of hay for better monitoring of carcass contamination and/or spoilage[1,7].

Botulism can be an intensive disease to treat with the possibility of many complications. Complications such as decubital ulcers, corneal ulcers, and aspiration pneumonia occur in about 60% of patients, but these do not have an adverse effect on survival[3]. There is typically a poor prognosis with an overall survival rate of 48% in treated horses[3]. However, there can be case success with horses, such as Ermac, that arrive standing and retain the ability to stand throughout hospitalization having a 95% survival rate. Ermac has been recovering well at home and is now able to eat dry grain and hay. His areas of decubital ulcers have healed nicely, and he is gaining weight.

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