A Case of *Clostridium botulinum* in a Warmblood Foal

Megan Born, BT., AAS., LVT

With attending Internists Nimet Browne DVM, MPH DACVIM, and Nathan Slovis, DVM DACVIM, CHT

Initial Presentation and Diagnostics:

A six-week-old warmblood filly foal presented to Hagyard Equine Medical Institute with a complaint of being recumbent. The only prior treatment done at the farm was a dose of flunixin meglumine. The foal's dam remained at the farm.

Physical and neurologic exams, a complete blood count, fibrinogen, chemistry and lactate analysis were performed. An ultrasound examination of abdomen and thoracic regions was performed.

On physical exam the heart rate was 80 bpm, respiratory rate was 24bpm, temperature of 101 degrees Fahrenheit. The foal had pink injected tacky mucous membranes with a capillary refill time of one second. Lungs sounds were audible with no crackles or wheezes present. Borborygmi were present in all four quadrants.

Her neurologic exam demonstrated ability to vocalize, move front and hind legs, normal anal tone was present, and the ability to move the tail was intact with reduced tail tone. The foal on admission had normal and consensual pupillary light responses. There was normal cranial nerve

examination with reduced eyelid and tongue tone. The foal was quiet and responsive but unable to stand without the assistance of three hospital personnel.

Ultrasonographic examination revealed no abnormalities other than an enlarged bladder.

The laboratory workup showed a normal white blood cell count of 5.7 K/microliter, all erythrocyte counts and indices normal, normal platelet amounts, slightly increased neutrophils and low lymphocytes, lactate in the normal range at 1.1 mmol/L (ref range 0.9-1.7 mmol/L), total protein normal at 6.1 g/dL (ref range 5.7-7.4 g/dL) fibrinogen was normal at 300 mg/dL (ref range 200-500mg/dL), Glucose was slightly high at 137 mg/dL (ref range 76-119 mg/dL) , lactate dehydrogenase was high at 555 U/L (ref range 112-408 U/L), and creatine kinase was mildly elevated at 634 U/L (ref range 120-320 U/L).

Initial attempts to stand during the first day demonstrated the foal becoming weaker over time. The foal was not able to sit sternal unless supported. Small amounts of hay were not able to be swallowed by the foal.

Case Differentials and Initial Treatments

Differentials included various types of neurologic diseases, infectious meningitis and trauma. The initial exams and laboratory work did not provide an immediate diagnosis; however, botulism antitoxin plasma was given to prevent further deterioration of the foal if the foal were to have *Clostridium botulinum.* Botulism antitoxin plasma type ABC (manufacturer Lake Immunogenics, NY) was given in the amount of 500mls.

A MILA polyurethane antimicrobial 16 gauge long term guidewire intravenous catheter was placed for the administration of antibiotics and fluids.

The foal was initially treated with intravenous ceftazidime due to the initial open diagnosis and its broad antimicrobial spectrum.

Most foals that are recumbent develop pneumonia which could be caused by either a gram positive or gram negative bacterium.

A 14 gauge foley catheter was placed vaginally into the urethra to assist with micturition.

Supportive replacement, maintenance fluids, and fluid additives were given. Normosol R was administered with dimethyl sulfoxide added due to its anti-inflammatory and diuretic properties. Calcium was also added to the fluids to enhance cellular and muscle function. Dextrose was added to the fluids as a caloric supplement as the mare was kept at home. Vitamin C was added to the fluids for its antioxidant properties.

The foal was placed on restricted orogastric intake.

The foal was placed on a tempurpedic mattress and turned every four hours to prevent lung atelectasis and decubital ulcers.

Artificial tears were placed in the foals' eyes periodically as botulism patients have reduced eyelid tone. Vitamin E was supplemented for its antioxidant properties that can help with nerve injury. Sucralfate was given to prevent ulcers. Orals were later discontinued due to foals weakened swallowing ability.

A primary differential of *Clostridium botulinum* was reached based on clinical appearance, exams, and behavior over the first 24-48 hours.

Clostridium botulinum **Etiology, Symptoms, and Geographic Distribution**

Clostridium botulinum in young foals is caused by the toxicoinfectious route of transmission. The foal becomes exposed to the bacteria as it starts foraging. In human babies and young animals with an immature gastrointestinal microbiota the bacteria are able to germinate in the gastrointestinal system. Type B toxin is typically implicated. Once these spores germinate they can produce toxins that cause the inhibition of acetylcholine at neuromuscular junctions. The most common form causes the inhibition of acetylcholine causes muscles to be unable to contract. It is important to note that only motor nerves are affected by *C. botulinum.* An affected foal still has sensory nerves and has the will to move or behave normally. Young foals usually less than 3 months of age have an immature intestinal microbiota that can allow these spores to germinate and proliferate in the gastrointestinal tract.

Older horses have a more mature intestinal microbiota and intestinal pH that are inhibitory for the spores to germinate in the intestinal tract.

Adult horses and older foals have to ingest toxin that is already formed in the forage (forage poisoning) to contract the disease. Horses can also contract botulism from toxin formation in deep penetrating wounds. Puncture wounds can cause bacterial growth of *C. botulinum* as it multiplies well in an anaerobic environment.

Foals affected by *C. botulinum* have a layman's term of Shaker Foals. They have acquired this name as diseased foals will stand and nurse and after one-minute start to shake and collapse on the ground without folding their legs normally.

The foal in this case study was a bit unlike some of these foals in that it would not shake but the indicative collapse and general muscle weakness was present.

Other clinical signs of botulism are muscle weakness, ileus, respiratory distress, weak eyelid tone, difficulty swallowing, weak or no tongue tone, mydriatic pupils or sluggish pupillary light responses, and in adult horses failure of the grain test. Cranial nerves are usually affected before other nerves.

Definitive diagnosis is often impossible in single cases. As a result, diagnosis and subsequent treatment of botulism is frequently based on compatible clinical signs, a compatible history of possible exposure to neurotoxin and ruling out other etiologies for observed clinical signs. Definitive diagnosis of botulism requires detection of neurotoxin in feed, serum, gastrointestinal contents or wound debris. Diagnostic tests include the mouse bioassay, ELISA, PCR test and use of an optical based biosensor. The mouse bioassay (MBA) is the gold standard laboratory diagnostic test for confirming a diagnosis of botulism through the detection of

botulism neurotoxin. 30% of adult horses with botulism are reported to have positive test results following culture enrichment using this assay. Recently, a quantitative real-time PCR has been validated for detection of neurotoxin genes of Clostridium botulinum types A, B & C in equine samples. Higher sensitivities for detection of Clostridium botulinum neurotoxin types A, B and C(89%, 86% and 96% respectively) compared to the MBA (81% sensitivity for neurotoxins types A, B and C) have been reported.

Botulism plasma cannot treat the neurons already affected by the toxins; it can only prevent more nerves from becoming affected. If the animal does not succumb to respiratory muscle paralysis or other complications during treatment the foal can form more neuromuscular junctions over a period of 10-14 days.

Foals that develop inadequate oxygenation and respiratory paralysis can be placed on a mechanical ventilator to expand the lungs and aerate the alveoli properly when the diaphragm is compromised. Adult horses that develop respiratory inadequacy are usually euthanized due to the inability of mechanical ventilators to support long term ventilation of large animals. Adult horses that are recumbent for more than a few days are at a high risk for mortality from developing debilitating myopathies, pneumonia, and ileus.

There are several types of botulism with botulism A, B, and C being most common in horses. Type B is the most prevalent of the three types with reportedly over 80% of cases being type B cases. The *Clostridium botulinum* toxoid vaccine protects against botulism type B. There are no vaccines for types C and A. Type B is found in most regions of the United States, type C in

prevalent in Florida, and type A is found in Western United States such as California, Idaho, and Oregon.

There is a conservative estimate of approximately 150-250 horses are infected with botulism per year which is higher than the human case rate at approximately 110 cases per year.

Progression of Recovery

The day after admittance the foal had objective observations of reduced muscle tone in the neck, less limb tone and no tail tone. The foal would move its legs but be unable to sit in sternal. Respiratory rate was 40bpm with more effort. Although it was able to swallow a little water, hay was restricted due to reduced deglutition ability. The foal was not defecating voluntarily and required enemas twice daily. A second 500ml bag of ABC botulism plasma was given intravenously. Metronidazole was started to be given per rectum. Pentoxifylline was added to the treatment regime for the anti- tumor necrosis factor to slow the inflammatory cascade. The foal was still getting its recumbency changed every four hours and standing the foal was temporarily suspended to help preserve acetylcholine. Ceftazidime was discontinued once meningitis was no longer suspected. Creatinine kinase and alkaline phosphatase remained high and electrolytes, CO2, and other bloodwork parameters were within normal limits.

Two days after admit intranasal oxygen insufflation was begun at a rate of 8L/min. Ampicillin was added to the treatment regimen to help treat the botulism which is susceptible to penicillin and to help prevent the foal from developing pneumonia. Total intravenous nutrition in a 3 liter bag with 70% dextrose (125.300 gm/L), 10% amino acids (Travasol 33.300gm/L), and 20% lipids (Intralipid 25 gm/L) and water (363ml/L) was started at a rate of 50ml/hr then gradually

increased to 150 ml/hr as glucose levels remained within normal range. The heart rate (bpm_ decreased to the sixties from the eighties. Respiratory rate (bpm) decreased to the twenties after intranasal oxygen was initiated. All oral medications were discontinued. Neopolybac was started to treat superficial eye ulcers. Epidermal abrasions were treated with silver sulfadiazine. Amino acids and dextrose were removed from the crystalloid fluids after TPN was initiated. The foal showed hyperesthetic behavior and could not sit sternal. The foal exhibited a low white blood cell count of 3.6K/L, bands were high at 7% of the total WBC count, lactate dehydrogenase was still increased, alkaline phosphatase was still elevated. Lymphocytes were analyzed at lower than normal. The client was informed that the prognosis for full recovery is

usually good (85%) as long as the foal does not develop a severe pneumonia or have to be placed

on a ventilator. However, they would be investing at least 1000$ USD per day.

Three days after admit the foal improved slightly and was able to sit in sternal for thirty minutes on its own. Pupillary light responses were improving and the foal was interested in trying to eat although oral ingestion was still restricted. The TPN was maintained at a rate to provide

the foal with approxiametly70% of its caloric needs. Metronidazole was discontinued since the ampicillin should have reached steady state by that time. The use of metronidazole has some controversy because it has been thought for toxicoinfectous botulism that metronidazole may cause the release of more toxins when it kills the germinated form of the bacteria. The foals CO2 was slightly elevated high at 39 mEq/L (ref range 25-32 mEq/L). total protein, hematocrit, lymphocytes, chloride, and creatine were all slightly lower than normal ranges.

On the fourth day after admission the foal was stood with assistance when turning and the foal was able to support some of its own weight for 2 minutes before collapsing. The foal was able to defecate with an enema assistance. Red blood cell indices were low. The rest of the bloodwork was similar to the previous day. Triglycerides were measured and found to be slightly high at 58 mg/dL (ref range 13-55mg/dL). Ammonia levels were measured and found to be normal. Potassium penicillin was started and ampicillin was discontinued. Flunixin meglumine was removed from serial administration.

On the fifth day another ultrasound examination of the lung fields was performed and comet tails were visualized with small areas of consolidation. Nebulization was started with Ceftiofur and Albuterol to bronchodilate and deliver antibiotics directly into the lower airways. Intranasal oxygen was still at a rate of 8L/min. The foal was able to pass manure on its own. CO2 levels were still just slightly over normal limits.

Over the next two days the foal after assist up with three people was able to remain standing for up to 6 minutes with support. The foal was able to take a few steps. She was able to swallow water without observable difficulty. Oxygen insufflation was reduced to 6L/Min. Ocular neopolybac was changed to artificial tears as the corneal surface lesions had resolved. Bloodwork remained similar with no concerning changes. A serum amyloid assay was done to detect early signs of pneumonia and the value was normal.

Seven days after admit the foal was started on 1/4 lb. of Wellsolve gel orally every eight hours. The foal was assisted to stand every 2 hours instead of every 4 hours and was still able to remain up for approximately five minutes each time. The foal began being able to walk around for short distances. Nebulization was reduced to BID instead of QID treatments. Bloodwork was unremarkable other than total protein being just under the reference ranges.

On the eighth day after presentation the foal was able to eat a senior type feed, soaked hay fines, and drink some water. Wellsolve gel was discontinued and the urinary catheter was removed.

Over the next few days, the foal continued to improve and total parenteral nutrition was discontinued. The intravenous catheter was removed. She was able to be turned out to the paddock for short times with support walking out. The foal was staying up for 15-30 minutes at a time. The pneumonia was improving and the foal was able to eat hay and sweet feed. Laboratory work remained fairly normal.

The foal stood without encouragement or assistance on the 14th day after admission and was staying up without assistance for 30 minutes at a time.

The foal was discharged to the farm on the 15th day after arrival. The clients had milked the mare during this time to maintain milk production and the foal was able to nurse from the dam without difficulty.

This case demonstrated the successful treatment of a foal diagnosed with *Clostridium botulinum.* The clients invested a significant amount (~17,000$) for the twenty four hour intensive care this foal required during 14 days of recovery. The coordinated effort of approximately twelve veterinarians and fifteen to twenty technicians contributed to the intensive care, diagnostics,

monitoring, and supportive treatments which prevented morbid complications of the disease processes of equine botulism.