What's Wrong Doc?

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Introduction

Equine Protozoal Myeloencephalitis (EPM) can be difficult to diagnose and treat. The clinical signs may also mimic that of other equine neurologic diseases making diagnosis challenging. The prognosis may vary and over 75% of treated horses will relapse (3). This can be very frustrating for equine clinicians as 76% of horses in the United States (99% in the southeastern) have some level of detectable titers for Sarcocystis neurona or 34% Neospora hughesli but less than 1% will be clinical for disease (6). This is a case review of a horse that had an uncommon presentation of EPM.

History and Presentation

Doc was an approximately 9-year-old quarter horse gelding who presented to the Mississippi State University College of Veterinary Medicine after hours equine emergency Service on Tuesday October 23, 2018. Doc's owners noted that starting on the 18th he was lethargic, slow to come in at night, and eating less. On 10/20/2018, Doc had profuse bilateral nasal discharge and the referring veterinarian was called for a suspected choke episode. On passage of a nasogastric (NG) tube, no obstruction was present. Fluids and electrolytes (unknown amounts) were administered via the NG tube. The next day, Doc was seen standing at the water trough frequently dipping his muzzle into the water but was never seen swallowing. At this time no other neurologic deficits were appreciated by the referring veterinarian and Doc was given Marquis at the 1000lb dose and a 0.05mg/kg dose of dexamethasone. Doc was administered medications, water, electrolytes, and pelleted feed via the tube over the next couple of days with no improvement.

There were 3 other horses and 100 head of cattle on the property, all were acting normal. Doc mostly lived on pasture and was stabled at night. He was supplemented with sweet feed and

ate pasture grass when available and Bermuda hay. He had a current Coggins and his teeth were last floated 2 years ago with no history of dental issues. Due to continued inability to eat, drink and abnormal mentation Doc was referred to MSU-AHC for further evaluation.

Diagnostic Approach

On physical exam, Doc was dull but responsive. His body condition score was 4/9 (5/9 is ideal) and he weighed 1000lb. His heart rate was 54bpm, respiratory rate was 12brpm, and rectal temperature 99.9F. On auscultation there was no cardiac murmur or arrhythmia. Harsh lung sounds were auscultated bilaterally with the right side sounding subjectively louder. Decreased gastrointestinal sounds was appreciated in all quadrants. Digital pulses were normal in all limbs. Doc had a low head carriage and bilateral mucopurulent nasal discharge. An oral speculum was placed and palpation revealed that the epiglottis could be appreciated caudal to the soft palate. This was highly suggestive that Doc had decreased masseter muscle tone. Doc additionally had normal tongue tone and movement. He had a moderate amount of edema in the intermandibular space that was not associated with lymphadenopathy. No pain was elicited on palpation of the neck and back. He had bilaterally symmetrical epaxial and gluteal muscle atrophy and was bilaterally weak on tail pull. His tail tone was mildly decreased but he had normal anal tone. His gait was normal at the walk and there were no obvious deficits in conscious proprioception. On ocular exam, slight cataract changes were seen but no pigment retinopathy was observed. Doc frequently adopted a base narrow stance (elephant on a ball stance) and stood tail against a wall.

A thoracic ultrasound was performed and revealed multiple broad based comet tails especially on the right side with milder changes on the left. Blood was drawn for serum Vitamin E levels, IFAT for EPM, a complete blood count (CBC), and biochemistry. The CBC and chemistry results: Hematology: WBC 13.10 (5-11.90), neutrophilia 12052 (2500-6000),

lymphopenia 786 (1250-5000). This signifies that it was likely that an active infection was taking place in Doc's body as well an underlying stress leukogram. Chemistry: Chloride 89 (98-106), CO2 35.6 (24-32), Glucose 172 (60-122), Globulin 5.4 (2.5-4.0). There is evidence of primary chloride-depleted metabolic alkalosis caused by Doc's excessive drooling, dehydration, and anorexia. A sedated upper airway endoscopy and gastroscopy were performed. Significant finds for the upper airway exam were that the soft palate was persistently displaced, even when manually placed in their normal anatomic relationship, they immediately displaced again. The walls of the pharynx lacked tone and sagged into the pharynx . The significant findings for the gastroscopy were severe gastric ulceration throughout the glandular and lower half of the nonglandular mucosa (Grade 5/5 non-perforating) and an infestation of *Gastrophilus intestinalis.* There was no evidence of mass, foreign body, or any mechanical cause of Doc's dysphagia meaning that a neurological cause was most likely. Hospitalization was recommended to provide nutritional support, antimicrobials, and await test results. A Mila enteral feeding tube was placed via endoscopy. The differentials at this time included: Equine Motor Neuron Disease (EMND) or vitamin E deficiency, EPM, Botulism, and Equine Degenerative Myeloencephalopathy (EDM), and lesser likely rabies.

Treatment and management

An intravenous (IV) catheter was placed in his right jugular vein. He was started on gentamicin 6.6 mg/kg IV every 24 hours and Naxcel 2.2 mg/kg IV every 12 hours to treat aspiration pneumonia. 500mls of Calcium Gluconate was added to 4500mls of Lactated ringers' solution (for a total of 5000mls in a bag) and 1.25L was given IV 4 times a day as long as Gentamicin was given. Misoprostol 5 mcg/kg was administered via enteral feeding tube (PO) every 12 hours. 4 mLs of ReBalance Antiprotozoal Oral Suspension per 110 lb (50 kg) of body

weight and Marquis (ponazuril) at 5mg/kg (1000lb dose) PO every 24 hours. He was fed a mixture of 2 scoops of Well-Gel, ¼ cup of corn oil and 2 Ls of fresh water every 4 hours. 2 scoops of Platinum Balance probiotic and 3mls of Elevate WS were added to this mixture every 12 hours. Electrolytes (15mls table salt, 5mls of light salt, and 20 mls of baking soda) in 5000mls of fresh water were given PO every 4 hours. He had physical exams every 4 hours for the first week of his hospitalization then was dropped to every 12 hours afterwards. Doc was seen laying down after his feedings.

A chemistry was performed on 10/25/2018 and the abnormal results were as followed: globulin 5.2 (2.5-4.0), magnesium 1.3 (1.6-2.5). This shows that the electrolyte imbalance was correcting. The oral electrolytes were discontinued, and he was switched to 4000mls of fresh water every 4 hours. His nasal discharge decreased after this day.

On 10/28/2018, Doc was spiking mild fevers thought out the day and his digital pulses were increased. His feet were iced and monitored throughout the night. A recheck CBC was performed on 10/29/2018 and the results were: WBC 14.80 (5.00-11.9), neutrophilia 13172 (2500-6000), lymphopenia 888 (1250- 5000). A recheck thoracic ultrasound was performed and showed complete consolidation of the right ventral lung such that it had the same echogenicity as the liver. The left side had more comet tails than on presentation. It was decided to switch antibiotics to chloramphenicol 50mg/kg every 6 hours via the enteral feeding tube. The serum Vitamin E results came back in the evening and the result was 8.4 (normal range 2.00-4.00). This ruled out EMND as a diagnosis.

On the morning of 10/30/2018, it was noted that Doc was no longer drooling excessively. This was the first indication that his swallowing reflex may be returning. Doc started to appear

more alert and able to lift his head up higher. He was still laying down frequently but appeared comfortable and his gut motility auscultated normally in all quadrants.

10/31/2018 the IFAT results for the EPM titers came in. Doc's titers for S. neurona was equal to or over 2560 and was negative for N. hughesli. The laboratory informed us that a titer over 640 had a 95% probability of an active infection of EPM caused by S. neurona. Doc's current medication plan remained the same. Daily 5-minute walks were added to his treatment as physical therapy to aid in his weakness and muscle atrophy.

On 11/4/2018, Doc was offered water soaked pelleted feed (1 scoop of Purina Senior in 1/2L of water). He was able to chew and swallowed without signs of choke. After a few hours, Doc started to show signs of discomfort (profusely sweating on his sides and tactile hyperesthesia.) He had normal gastrointestinal motility and he was monitored closely for signs of colic. Sucralfate was administered orally every 8 hours from this point until discharge. Later that night, he retroflexed the Mila tube out through his mouth so the tube was removed, and all his medications were given orally, and his feedings were increased. Hydrohay was added to his feeding regime.

On 11/9/2018 a repeat ultrasound of Doc thorax was performed and showed the pneumonia was 90% resolved with only a few comet tails in the right cranioventral lung field and no evidence of consolidation. Repeat CBC and chemistry were performed:
chemistry: Globulin 4.3 (2.5-4.0), OSMO 267 (270-300), Tbili 3.6 (0.2-3.5). Hematology: Neurophilia 8369 (2500-6000), Lymphopenia 1154 (1250-5000). The time and frequency increased as he became stronger. Doc was taken outside to graze on fresh grass during some of his walks. Flunixin meglumine 1.1mg/kg was started to help with any inflammation affecting his nerves.

Pathophysiology of EPM

The protozoa are introduced to the horse by consuming contaminated feed or water (3). The sarcocytes undergoes schizogony in the extraneural tissues before entering the central nervous system (CNS) as sporozoites (1). The schizonts can be found in various stages of maturation in a neuron. Horses have low numbers as they are an aberrant host but in other species can be as many as hundreds in a single neuron (3). Most horses are affected in the spine and show signs that are commonly asymmetrical, atrophy of muscles, and ataxia of one or all legs (1). In cases where the brain or cranial nerves are affected, the most common clinical signs are: head tilt, depression, facial nerve paralysis, difficulty swallowing, upper airway dysfunction such as dorsal displacement of the soft palate and laryngeal hemiplegia have been noted although signs are not limited to these (1). In the case of Doc, his brain stem was most likely affected or at least one of the cranial nerves associated with swallowing. These signs are due to the pathogen as well as the inflammatory process. His clinical signs more closely resembled those of EMND (muscle wasting, muscle fasciculations, prolonged recumbency, shifting weight while standing, a short-strided gait, and a base-narrow stance, elevated tail head carriage, low head and neck carriage, profuse sweating, a ravenous appetite, and a brown pigment retinopathy) (2).

Diagnostics

Definitive diagnosis antemortem is very challenging. Clinical signs can mimic those of other neurologic diseases as with Doc since the primary differential was EMND. Blood work and Cerebral Spinal Fluid (CSF) analysis are mostly unrewarding as the protozoan typically doesn’t cause direct change in these (7). Horses typically have lower number of organisms to cause clinical disease, so it is rare to see merozoites in the CSF (1). PCR has been shown to

have a lower sensitivity as there are not may organism so is more used as a post mortem test (1). Most commonly used diagnostic is serologic testing using Western Blot (SAT and the IFAT). The gold standard diagnostic is serum:CSF ratio using ELISA SAG 1,2,3/4,5,6 but many times is not performed as it is difficult to obtain CSF from affected horses (8). C-Reactive protein or serum Amyloid A did not aid in diagnosis (7). It is important to rule out other disease processes before diagnosing EPM antemortem as titers only indicate past exposure to the pathogen and have a long half-life (1).

Postmortem diagnosis relies on gross lesions, microscopic lesions, and immunohistochemical staining. Gross acute lesions typically show multifocal, randomly-distributed foci of hemorrhages and chronic lesions show areas of discoloration ranging from pale to dark tan areas and foci of malacia (1). Lesions are most commonly seen in the spinal cord, then the brain stem, then least commonly in the other areas of the brain (1). Microscopic lesions are most likely to be multifocal to coalescing areas of hemorrhage, nonsuppurative inflammation, and small foci of necrosis. Perivascular cuffing by mononuclear cells is evident frequently in the meninges (1). Immunohistochemistry may or may not reveal any organism as stated before there are not as many organisms present in a horse (1).

Treatment and Management

Typical treatment of acute cases involves decreases the inflammation to the CNS, giving an appropriate antiprotozoal, and treating any additional sequala of the disease. Horses are treated aggressively with DMSO, phenylbutazone, anti-inflammatory dose of steroids. The antiprotozoal treatments that are proven to have affect and are safe: ponazuril (5 mg/kg/day, PO, for at least 28 days), diclazuril (1 mg/kg/day, PO, for at least 28 days), and a combination of sulfadiazine and pyrimethamine (20 mg/kg and 1 mg/kg, PO for at least 90 days). Some

clinicians will continue to give the anti-protozoals until the titers responds to treatment, while other will continue treatment until resolution of clinical signs. Approximately 60% of horses with EPM diagnosis improve with treatment, but <25% recover completely (3). Relapses occur commonly up to 2 years after discontinuation of antiprotozoal therapy (3).

Prevention

Prevention is done by minimizing risk of exposure to the organism. This means fresh water and keeping feed in closed containers to eliminate the risk of contamination. There are no vaccines or preventatives on the market currently (4). As most horses in North America have some titers to S. neurona, it is thought that horses that are immunocompromised are more at risk for showing clinical signs (1). In mice, Interferon Gamma is important for controlling infection and when this was absent the mice became clinically infected (1). It is not recommended to give all horses on a property treatment (3). It is also not recommended to test all horses on the property either as it is seldom that multiple horses on a farm are affected (1). This is a disease that should only be treated when clinical signs are present.

Case Outcome

On 11/10/2018 ultrasound was performed which showed normal lung echogenicity and no pathology. Doc was discharged on 11/11/2018 at 7:30am with instructions to continue the Rebalance and Marquis. He was given 6 more days of chloramphenicol, 14 more days of Misoprostol, and 7 days of flunixin meglumine. Doc's owners elected to do initial follow up with their primary veterinarian. On further calls, his owners informed us that he was doing very well at home. One year after presentation, Doc returned for a recheck examination and no neurologic deficits were detected. His muscle atrophy was resolved and he had gained over 100lbs.

References

(1) Dubey, J P et al. “An update on Sarcocystis neurona infections in animals and equine protozoal myeloencephalitis (EPM).” *Veterinary parasitology* vol. 209,1-2 (2015): 1-42.

(2) Husulak, Michelle L et al. “Equine motor neuron disease in 2 horses from Saskatchewan.” *The Canadian veterinary journal = La revue veterinaire canadienne* vol. 57,7 (2016): 771-6.

(3) MacKay, Robert J., and By. “Overview of Equine Protozoal Myeloencephalitis - Nervous System.” Merck Veterinary Manual, Merck Veterinary Manual, 1 Nov. 2019,

(4) Saville,William J.a.,et al.“Testing the Sarcocystis Neurona Vaccine Using an Equine Protozoal Myeloencephalitis Challenge Model.”Veterinary Parasitology,vol.247,2017, pp.37–41.

(5) Hay, Alayna N., et al. “Sarcocystis Neurona–Induced Myeloencephalitis Relapse Following Anticoccidial Treatment.” Journal of Parasitology, vol. 105, no.2,2019, p. 371.

(6) James, Kaitlyn E., et al. “Seroprevalences of Anti-Sarcocystis Neurona and Anti-Neospora Hughesi Antibodies among Healthy Equids in the United States.” Journal of the American Veterinary Medical Association, vol. 250, no. 11, 2017, pp. 1291–1301.

(7) Mittelman, Neil S., et al. “Utility of C-Reactive Protein and Serum Amyloid A in the Diagnosis of Equine Protozoal Myeloencephalitis.” Journal of Veterinary Internal Medicine, vol. 32, no. 5, 2018, pp. 1726–1730.

(8) Mittel, Linda, et al. “Equine Protozoal Myeloencephalitis (EPM) Testing.” *Cornell University College of Veterinary Medicine*, Cornell University College of Veterinary Medicine, 18 Jan. 2011, www.vet.cornell.edu/animal-health-diagnostic-center/testing/protocols/epm.