White and Maladjusted

- A Tale of Two McGees -

Clinicopathologic Conference

March 4, 2022

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Class of 2022

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Signalment

McGee or “Mystic’s Foal” was a 12-hour old, solid white, Thoroughbred colt that presented to MSU-CVM Equine Medicine and Surgery Service on emergency basis for inability to stand and failure of passive transfer.

History

McGee presented to MSU-CVM Equine Medicine and Surgery on emergency basis on 8/17/2020 for inability to stand and failure of passive transfer. McGee’s dam, Mystic, had been bred and recently purchased in Canada and had been shipped to her owner’s hauler in Alabama before having her foal. Mystic had a history of chronic founder and was being treated with phenylbutazone throughout her pregnancy. She had been treated with Bute-Less for the final month of gestation. McGee was born approximately one week early from his expected due date without complication; however, the fetal membranes were noted as discolored and foul smelling once passed. McGee did not exhibit normal neonatal behavior and was neither able to stand nor nurse appropriately. Mystic was unable to be trailered to accompany her foal to the CVM due to severe founder. Thus, McGee presented alone after having received an unknown amount of Exceed and being orally fed sugar water in route to the Equine Unit.

Diagnostic Examination

Upon presentation, the foal was dull, weak, laterally recumbent, and nearly comatose. He weighed 36.6 kg (80lbs). His rectal temperature was 99.3*F, his heart rate was 80 bpm, and his respiratory rate was 24 brpm. Thoracic auscultation revealed normal bronchovesicular sounds, no arrhythmias or heart murmurs. He was severely dehydrated and exhibited cutaneous contusions on his face (cranial to his eyes), elbows, flanks, and hocks due to suspected poor

perfusion. His mucous membranes were slightly icteric with moderate scleral injection, bilaterally. Entropion of the lower palpebrae was notable bilaterally. The ears were drooped and floppy with aural cartilages soft on palpation. Eponychia were intact and present on all four hooves. The coronary bands were dark and exhibited a slightly purple hue. Laxity was noted in his fetlock and pastern joints. The foal was unable to voluntarily support his head.

Initial bloodwork revealed marked leukopenia (WBC count of $1.48x10^3$ cells/uL (5.0 – 11.9 $x10^3$) characterized by severe neutropenia (162.8/uL (2500 – 6000) confirmed on blood smear. Marked hypoglycemia was present with a blood glucose of 20 mg/dL (60 -122). Total CO2 was decreased at 18.8 mEq/mL (24-32) and blood pH was 7.2 (7.35 – 7.46) denoting severe metabolic acidosis. Serum lactate was found to be inconsistent with life at 14.7 mmol/L (0.5 – 2.5 mmol/L) and CK was markedly elevated at 2753 U/L (57-283 U/L). The serum IgG was analyzed and found to be <400 mg/dL (with normal passive transfer levels >800 mg/dL) indicating marked failure of passive transfer.

Fluorescein stain was performed four days after the foal presented due to unresolving bilateral entropion. Illumination with blue light revealed bilateral corneal abrasions present directly over the pupils. Once the foal was able to stand on his own consistently (approximately 10 days into hospitalization), it was noted that he leaked urine from his umbilicus, especially when posturing to urinate. Abdominal ultrasound confirmed presence of a patent urachus along with a mild amount of free fluid present around his umbilical vessels. The contusions present on McGee's elbows, shoulders, hips, and hocks noted upon initial physical exam progressed to pressure sores and eventually to open wounds as his skin sloughed from the areas. Successful treatment of these wounds revealed itself to be a very lengthy undertaking as detailed below.

During the first two weeks of the foal's extended tenure in the equine unit, he continued to exhibit very abnormal behavior for a foal. He was mentally dull, unable to roll into sternal position, flailed his head and limbs, urinated and defecated in lateral recumbency, and struggled to maintain balance or place adequate weight on his limbs when supported in a standing position. His presentation as well as continued dullness allude to his diagnosis with Neonatal Maladjustment Syndrome, colloquially termed Dummy Foal. The white coloration and tumultuous neonatal period was somewhat suspicious of Fatal White Overo Syndrome, or Ileocolonic aganglionosis, however his brown irises and ability to defecate assuaged initial concerns.

Pathophysiology

Neonatal Maladjustment Syndrome, also known as Dummy Foal Syndrome or Neonatal Encephalopathy, is a condition of postnatal foals that is characterized by inappropriate mentation, poor awareness, poor suckling behavior, decreased affinity for the mare, and/or generalized hypotonia (6). Those with the ability to ambulate are often referred to as "Wanderers" or "Barkers" as they often meander away from their mares and may exhibit abnormal vocalization. Affected foals may appear normal at birth before developing clinical signs (2). Severely affected foals may suffer marked central nervous system abnormalities including dysregulation of core body temperature, blood pressure, and respiration. Furthermore, NMS often affects the GI tract and has been known to not only cause functional ileus and colic but can result in necrotizing enterocolitis. This condition arises from gastrointestinal ischemia decreasing appropriate mucous production and resulting in autolysis of the mucosa by proteolytic enzymes present within the intestines. Bacterial invasion of the intestinal tissues then leads to enterocolitis and possible sepsis if medical intervention does not occur (2). NMS has been found

to occur more frequently in foals birthed by mares with reproductive tract disease (placentitis, hydrops allantois, prepubic tendon rupture), endotoxemia, anemia, or hypoproteinemia.

Although the pathophysiology of NMS is still somewhat contested, several potential inciting causes have been hypothesized to be responsible for the condition, including placental insufficiency, hypoxic birthing conditions, acute ischemic events within the brain during parturition, and inappropriate concentrations of circulating neonatal progestogens. Early on, NMS was believed to be caused by acute ischemic events occurring during parturition. One 1976 study, conducted by the Cambridge School of Veterinary Medicine, found that in eighteen foals with signs of NMS, nine exhibited ischemic necrosis of the cerebral cortex and three exhibited necrosis of the diencephalon and brainstem. The remaining nine animals had acute hemorrhage within the brain, and four foals also had cerebral edema present upon necropsy (4). The study theorized that dummy foals were born and/or gestated under hypoxic conditions leading to the neurologic signs (4).

More recent research conducted in 2013, found that pregnane steroid hormone concentrations decreased significantly over the first 48 hours of life in healthy neonatal foals but remained increased in ill foals and foals with Neonatal Maladjustment Syndrome; correlating increased pregnane levels with delayed transition from intra-uterine to extra-uterine life (5). During in-utero development, fetal unconsciousness (which both reduces oxygen requirements and keeps foals from “galloping in the uterus”) is maintained by a litany of neuroinhibitory compounds, including adenosine, progesterone, allopregnanolone, pregnanolone, prostaglandin D2, and placental peptides (8). Pressure on the fetus occurring during Stage-2 labor stimulates release of powerful neuroactivators such as estradiol-17β and noradrenaline, which subsequently reduce circulating neuroinhibitory concentrations and prime the brain for arousal to postnatal

consciousness (8). A 2012 study found that experimental allopregnanolone infusion in healthy neonatal foals produced the same neurobehavioral alterations as seen in foals born with Neonatal Maladjustment Syndrome via action on $GABA_A$ receptors within the CNS (3). The most current understanding of this condition is that it is caused by an interplay of abnormal birthing conditions, external environmental stimuli (such as temperature, visual, auditory, and olfactory inputs), changes in physical compression of the fetus during labor, and increased neuromodulating hormone concentrations in the foal following birth (6).

Interestingly, healthy neonatal foals exhibit rapid unconsciousness and NMS-like "squeeze-Induced somnolence" when manual pressure is applied to their body, a phenomenon colloquially referred to as "flopping response" (6). Experimental evidence has shown that application of a rope restraint device results in lateral recumbency, sleepy behavior, decreased TPR values, and significant surge in circulating neurosteroid hormone concentrations (7). This procedure was theorized to simulate the passage of the foal through the birth canal during parturition and gave rise to the Madigan Squeeze technique developed as a potential treatment for NMS. This technique was contrived by Dr. John E. Madigan in conjunction with UC Davis School of Veterinary Medicine and has experimentally been found to decrease the recovery time of dummy foals. NMS foals that were squeezed for 20 minutes without other medical therapies were 17.5x more likely to recover within 24 hours than the group of foals receiving only medical therapies (6). Neonatal Maladjustment Syndrome carries a good prognosis with approximately 80% of affected foals recovering with medical intervention and/or squeeze therapy, however more research is needed to fully understand the cause of this condition.

Treatment

The foal underwent intensive treatment in hospital and was closely monitored and accompanied 24/7 during the first two weeks of his hospitalization. During his initial triage, a catheter was placed in his left jugular vein and he was bolused 1000mL of LRS with 100 mL of added 10% Dextrose solution in order to begin correcting his dehydration and hypoglycemia. LRS and Dextrose CRI's were titrated to effect using blood glucose readings. During his first night in hospital, the foal received a 1L equine plasma transfusion to correct his low serum IgG. Serum IgG concentration was checked every 24 hours for the first 5 days of hospitalization to ensure levels remained >800 mg/dL. No complications occurred and no additional transfusions were required.

The foal was unable/unwilling to suckle a nipple to facilitate bottle feeding, thus a naso-esophageal tube was placed via his left nostril for feeding and drug administration. He was fed approximately 20% of his body weight per day with warmed "Mare's Match" milk replacement administered via his NE tube every 2 hours. Due to his leukopenia, FPT status, injected sclera, and discolored coronary bands, intravenous antibiotic therapy was initiated with ampicillin and amikacin administered every 8 hours and every 24 hours, respectively. Early in his hospitalization, the foal suffered from severe, liquid diarrhea and was treated with Biosponge, sucralfate, and Gastroguard administered via his NE tube. His diarrhea improved significantly with gastroprotectant and antibiotic therapy and had resolved by day six in hospital. Antibiotic therapy was changed to oral chloramphenicol after 10 days of amikacin administration. The umbilicus was dipped in 50% chlorhexidine solution every 6 hours to sanitize and dry the umbilical stump site.

Triple Antibiotic Ointment was administered into both eyes every 4 hours beginning at his initial presentation as both eyes were very inflamed. Entropion was monitored for signs of improvement. However, when the condition had failed to improve and had been shown to be abrading the surface of the cornea, stay sutures were placed under sedation in the lower palpebrae to evert the eyelids and correct the entropion. Triple antibiotic therapy was continued until resolution of the corneal abrasions and entropion.

In an effort to reduce the incidence of bed sores, the foal was kept on an ICU cushion and turned every two hours. Due to the inability to roll into sternal position or stand, he had to be consistently cleaned with baby wipes and dry shampoo as he defecated and urinated. Regardless of turning and near constant cleaning, the contusions present on the elbows, shoulders, hips, and hocks continued to worsen. As previously mentioned, the sites quickly progressed to sores. The sores were cleaned and treated with silver sulfadiazine cream four times daily. Intermittent fevers of 102-103*F arose and signs of severe inflammation at the site of the sores worsened as wound care with SSD cream was continued. Due to an allergic reaction to the sulfa cream, SSD cream was discontinued in favor of flushing with sterile saline and application of triple antibiotic ointment. Use of sulfa drugs was carefully avoided for the remainder of hospitalization. The skin of the sores present on the elbows and hocks had mostly sloughed away by the time the SSD was discontinued. The sites were surgically debrided under sedation and tenderly scrubbed with dilute chlorhexidine solution. Bandages were placed over the sores and were changed every 2 days to decrease contamination and monitor healing. TrizEDTA cream with added 10% Gentamycin was found to have great benefit on the healing of the chronic sores. The wounds present on the hocks persisted for the remainder of his stay in hospital and underwent open

wound management with bandaging, TrizEDTA, and cefaparin topical therapies as surgical closure was unable to keep the wounds closed.

A Madigan Squeeze technique was performed on day 9 to address his continued struggle with abnormal behavior a la Fetal Maladjustment Syndrome. He had shown great effort in attempting to roll into sternal recumbency and was able to "ambulate" with much support, taking his "first steps" so to speak on day 6 of hospitalization. However, he continued to be mentally dull, and held his head low as he stumbled around his stall. To perform the procedure, a halter rope was passed over his shoulders and around his chest and abdomen and was squeezed tightly for 20 minutes to simulate passage through the birth canal. The foal's condition did not drastically resolve after the procedure; however, his clinical signs did appear to improve after the Squeeze had been performed. The foal became noticeably more mentally bright and by day 10, he was able to stand and walk by himself. He continued to grow stronger and improve in his ability to stand up on his own, ambulate for longer periods, and lay down without assistance. Improvement in the patient's condition was slow but steady. He began to show some interest in lapping milk replacer when offered from a bucket on day 10 and was introduced to bottle feeding with warmed "Mare's Match" on day 12. The foal exhibited great difficulty in properly creating a seal with the bottle's nipple and would often cough after attempted feedings. Evidence of aspiration pneumonia was found on thoracic ultrasound as coughing persisted. Interestingly, the foal's blood selenium level was found to be below reference range for horses (145 ng/mL (ref. 160 – 275 ng/mL)) and his difficulty in swallowing properly was attributed to this selenium deficiency. Subsequent selenium supplementation was found to resolve his difficulty bottle feeding. The foal was continued on chloramphenicol antibiotic therapy to address his aspiration

pneumonia and would continue to be fed through a combination of bottle feeding and via his NE tube until he was able to handle a diet of Bermuda grass hay and grain.

Case Outcome

In all, McGee remained in hospital for 236 days. He was treated for Fetal Maladjustment Syndrome, Failure of Passive Transfer, entropion, chronic wounds of his elbows and hocks, aspiration pneumonia, cellulitis of the right hock, and physitis while hospitalized. McGee was discharged on April 9, 2021 with instructions to continue coverage of his healing hock wounds, details covering careful turn-out and monitoring of his heat intolerance (due to suspected partial anhidrosis), and recommendations for socialization with other horses. Attempts to contact McGee's owner for update have thus far been unsuccessful. McGee's current whereabouts and condition is currently unknown.

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