“A Pain in the…”

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College of Veterinary Medicine
Class of 2021

Clinicopathological Conference
September 4, 2020

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Introduction

Exertional Rhabdomyolysis can be classified as a syndrome that is spurred by exercise-induced muscle damage that leads to increased serum levels of aspartate transaminase (AST) and creatine kinase (CK). There are two categories of exertional rhabdomyolysis (ER), acute and chronic. Acute ER is characterized by a set of circumstances leading to an event while chronic ER has one or multiple genetic component(s) that lead to several events of ER. While acute and chronic ER have varying causes, both present similarly. The following case will focus on acute ER in a quarter horse gelding, and his recovery after treatment.[6,2,3]

History & Presentation

An 11-year-old quarter horse gelding presented to MSU CVM Equine Surgery service for lameness of the hindlimbs on March 19,2020. That morning, the gelding was exercised aggressively then rested abruptly. Following the rest, he was reluctant to move. The gelding is used for working cows, housed in a stall, and is up to date on vaccines and Coggins.

Upon presentation, he was bright, alert, and responsive. He weighed 1103 lbs with a body condition score of 5/9 (4-5/9 being ideal). His mucous membranes were moist and pink with a capillary refill time of less than 2 seconds. His temperature was 99.7 degrees Fahrenheit, heart rate was elevated at 60 beats per minute (normal is 20-40 bpm), and respiration rate was elevated at 40 breaths per minute (normal is 10-20 bpm). His gut sounds were normal on the right side and decreased on the left side. His gait was stiff at the walk. He stood with his back arched and a wide hindlimb stance. Normal digital pulses were palpated in all four limbs. Muscle fasciculations were present over both sides of the abdomen, flank, and chest. The muscles of his caudal thighs were sensitive and very firm on palpation, more so on the left side.

Diagnostic Approach

Due to the decreased gut sounds, abnormal vital parameters, and the sensitive nature of horses, the gelding was evaluated for colic. A nasogastric tube was placed, and he produced no net reflux. Half a gallon of mineral was administered through the tube, then the tube was removed. A blood sample was collected for a complete blood count (CBC) and a serum chemistry panel. CBC revealed a mild stress leukogram; neutrophilia-7242/ul (2500-6000) and lymphopenia-1022/ul (1250-5000). Serum chemistry revealed hyperglycemia-169 mg/dl (60-122), creatinine-2.1 mg/dl (1.2-1.9), AST-3270 U/L (134-406), hypophospatemia-2.2 mg/dl (2.4-4), OSMO-261 mOsm/kg (270-300), and CK-79720 U/L (57-283). CK is the most specific enzyme for skeletal muscle damage. It reaches its maximum concentration approximately 12 hours after an incident and quickly declines 24-36 hours post incident. The CK was markedly elevated and may not have even reached its peak at the time of blood sampling. This level indicates that muscle damage did occur and that it was an acute incident. AST is another muscle enzyme which reaches max concentration at 24-36 hours after an incident and is slower to return to normal taking 2-3 weeks. The remainder of the blood work was insignificant. Red tinged urine was observed on presentation. The pigmentation of which could have been due to presence of myoglobin or hemoglobin; however, urine was not collected and analysis for differentiation was not performed. Myoglobin was highly suspected as it would be released in the face of severe muscle damage. Considering the history, presentation, bloodwork values, and discolored urine, acute (sporadic) exertional rhabdomyolysis was diagnosed.

Pathophysiology

Acute (sporadic) ER patients typically have a history of an increase in exercise regime than the horse is trained for, exercise while the horse is ill, an introduction of exercise following

a period of rest for the horse, heat exhaustion, or nutritional imbalances. There is no breed, age, or gender that is more predisposed to acute ER. Horses can present with reluctance to move, sweating, muscle fasciculations, ataxia, increased heart rate, and labored breathing.[6] Episodes of ER may not always have obvious signs, and horses may present with a history of lower performance, uncomfortable muscles, or hesitance to collect. While clinical signs are suggestive, a serum chemistry should be performed to evaluate CK and AST values. If those values are elevated, a diagnosis of ER can be made. The higher elevations of CK and AST can be explained by degree of muscle damage or amount of time passed since the onset of damage. In severe cases, electrolyte abnormalities may be present because of excess sweating and muscle damage. When ER is severe enough, it can cause myoglobinemia and myoglobinuria, which is released from myocytes following damage. Myogolbinuria is toxic to the renal tubules and can lead animals to azotemia or renal failure. [2,3] Renal compromise is possible in cases of ER because of the ischemic and nephrotoxic effects of myoglobinuria, dehydration, and use of NSAIDs.[2]

Overexertion is characterized by an increase in workload or intensity that the animal is not properly trained for or adjusted to. Signs associated include muscle rigidity, gait abnormalities, and moderate elevations of CK. When muscle biopsies were taken and analyzed in such cases, light microscopy did not reveal any pathologic changes where electron microscopy revealed interruption of the arrangement of contractile proteins within fibers. Muscle biopsies taken from horses that were simply overworked, revealed pathologic changes where there was more muscle-size fiber variation and centrally located nuclei of the muscle fiber.[6]

Horses who work in hot and humid weather are susceptible to heat exhaustion. Signs of which include muscle tremors, weakness, increased respiration rate, sweating, and loss of

consciousness. Horses may have an elevated body temperature, non-firm muscles on palpation, with or without myoglobinuria.[6,2]

Dietary imbalances include high non-structural carbohydrates, low amounts of selenium and vitamin E, or electrolyte imbalances. Concentrations of vitamin E and selenium can be measured to determine deficiencies. ER horses are uncommonly deficient in selenium, and there is little evidence that supplementation will aid in the prevention of future ER episodes. Electrolyte abnormalities may include hyponatremia, hypochloremia, hypocalcemia, hyperkalemia, and hyperphosphatemia. When a horse sweats, fluid and electrolytes (sodium, chloride, and calcium) are lost to the environment. These products are also lost to a shift down a concentration gradient into damaged myocytes. Damaged muscle will discharge potassium and phosphorus into circulation. In cases of hypochloremia, a compensating metabolic alkalosis may result.[6,2,3]

Treatment

The mainstay of ER treatment is decreasing anxiety and muscle pain while correcting fluid deficits and electrolyte abnormalities. While not necessary in this case, sedation and analgesia can be used to keep the horse calm. Examples include, acepromazine (0.04 – 0.07 mg/kg), xylazine (0.2– 0.5 mg/kg), or detomidine (0.02– 0.04 mcg/kg) combined with butorphanol (0.01– 0.04 mg/kg). Horses experiencing significant pain can be placed on detomidine, lidocaine, or butorphanol constant-rate infusion (CRI).[2]

Non-steroidal inflammatory drugs (NSAID) can be used as pain management. Examples include ketoprofen (2.2 mg/kg), phenylbutazone (2.2– 4.4 mg/kg), or flunixin meglumine (1.1 mg/kg). In dehydrated animals, NSAIDs are contra-indicated. When administered to a

dehydrated horse, NSAIDs can prevent the body's compensatory mechanisms for perfusion, causing gastric ulcers and kidney damage. Dimethyl sulfoxide (DMSO) can be administered as a free radical scavenger, anti-inflammatory, and osmotic diuretic.[6]

When animals are recumbent, methyl prednisolone succinate (2– 4 mg/kg, IV) has been successful in the acute phases. Methacarbamol (5–22 mg/kg, IV, slowly), a muscle relaxant, has shown dose-dependently positive results. Dantrium sodium (2-4 mg/kg, orally) can decrease muscle contractions and potentially prevent further muscle death by decreasing release of calcium from the sarcoplasmic reticulum. It can be redosed every 4-6 hours, but it is absorbed better after a minimum 3 hour fast.[2] Caution is necessary as overdosing can lead to muscle weakness. This is especially important with HYPP animals where increases in serum potassium can lead to an episode. The gelding in this case was not showing severe enough signs to warrant the treatments above.[6]

Horses that are mildly dehydrated can be supplemented through oral or nasogastric administration of electrolytes and water. Intravenous (IV) administration of balanced polyionic electrolyte solutions are utilized in severe cases of ER. When hyponatremia, hypochloremia, and hyperkalemia are present, isotonic saline, 2.5% dextrose, or 0.45% saline may be indicated. When hypocalcemia is present, adding 100-200 ml of 24% calcium borogluconate is recommended. Fluid replacement should be based off level of dehydration, and continued hydration status should be monitored via packed cell volume, total protein, and electrolyte derangements. Blood urea nitrogen and creatinine levels should be monitored as indicators for renal function. Recumbent animals require more nursing care, such as deep bedding, prevention of damage to the eyes, decubital sores, and intermittent turning. Horses with ER should be stall rested on a strictly hay diet for several days. [6]

Upon presentation, an IV catheter was placed in the gelding's left jugular vein using aseptic technique, and he was bolused 20 liters (L) of a balanced Hartman's solution, which was then reduced to a rate of 2L/hour. The gelding was hospitalized from March 19,2020 to March 23,2020. Flunixin meglumine (1.1 mg/kg) was administered IV q24 for the duration of his stay. Dimethyl sulfoxide (480 ml with 5L of Hartman's solution) was administered IV q24 for the first 3 days of his stay. During his stay, he was restricted to stall rest only to prevent further muscle damage. He was maintained on IV fluids for the first 3 days. He was administered 30 cc of salt q24 once his fluids were discontinued to promote oral consumption of water. Bloodwork was monitored q24 until the day before he was discharged. His elevated CK and AST values continued to decrease throughout his stay, and his renal values remained within normal levels throughout his stay. The red-tinged urine progressed to a normal color during his stay. These are indications that medical management was successful in treating the disease as well as protective of further damage.

On March 22,2020, the gelding developed a temperature of 103.6 (normal 99.5-100.5) that was due to phlebitis from his jugular catheter. While the catheter was placed as aseptically as possible, there is always a chance of complications such as inflammation and infection. The catheter was removed and wrapped with a triple antibiotic ointment. Bloodwork was submitted to determine the degree of insult or if there were any other systemic abnormalities resulting in the fever. The bloodwork was unremarkable, apart from the elevated muscle enzymes although they proved to be trending towards returning to normal. He was started on oral trimethoprim sulfadiazine (Uniprim 2 scoops poq12), oral aspirin (1/4 scoop poq24), topical anti-inflammatory cream (1% diclofenac sodium), and hot packing of the site. TMS is a broad-spectrum antibiotic that is bactericidal to common staphylococcus and streptococcus organisms

that were most likely the cause of the infection. Hot packing is used to keep the swelling and inflammation down while he was recovering. Surpass (1% diclofenac sodium): Surpass is a topical anti-inflammatory that will reduce swelling and inflammation of the previous catheter site. Aspirin can be used for its analgesic, anti-inflammatory, and antiplatelet effects. In this case, it was being administered mainly to prevent the formation of a thrombus in the left jugular vein.

Phlebitis is a common complication of large bore, long-term indwelling catheters. The jugular vein is commonly used for catheter placement in horses. Large bore catheters, 14 gauge, are used for swift administration of IV fluids for patients in critical condition. Long-term catheters are made of polyurethane which can be maintained for several weeks. Aseptic technique is utilized while placing the jugular catheter to limit the amount of contamination to the vein.[4,5] Proper catheter maintenance includes changing injection caps daily, flushing the catheter every 4 to 6 hours with heparinized saline, flushing the catheter before and after each drug administration, and changing heparinized saline syringes daily. The catheter site should be checked every 12 hours for heat, swelling, and pain. When phlebitis does occur and is recognized, the catheter should be removed immediately. Phlebitis will typically resolve with regional therapy, such as heat packing, topical dimethyl sulfoxide, and monitoring. Ultrasound can be used to detect fibrin strands within the vein, which would necessitate systemic antibiotics.[4] Studies show that bacillus and staphylococcus are the most isolated from the tips of catheter upon removal. [5] Phlebitis can cause pyrexia and a change in neutrophil count.[4]

Management

After treatment of acute ER and return of flexibility, confinement to a small paddock is recommended until serum CK levels are back to normal. The first 2 weeks immediately following treatment are critical because that is the time where horses are more susceptible to re-

injury. The limited space allows horses to decide their own exercise, which frequently avoids further damage. If paddock turnout is not available, careful hand walking of no more than 5 minutes a day may be performed as an alternative. Diet should be assessed to ensure the food contains a recommended amount for the intensity of exercise. If the manufactured feed is too high in calorie for the horse, then a lower calorie diet that has balanced vitamins and mineral should be utilized. A salt block may be made available to offer additional sodium chloride depending on the level of heat, humidity, and exercise regime. Once CK is within reference range, exercise can gradually be reintroduced, starting with 20 minutes of less of work a day until the horse is meeting the routine amount of exercise.[6]

Case Outcome & Conclusion

Prognosis is directly related to degree of clinical signs and renal impact. Horses, like the gelding in this case, who show moderate signs of discomfort, are recognized, are treated early, and are still mobile will have a good prognosis when the owner is willing to make the necessary changes. Horses who are recumbent, and have inadequate renal response tend to have a poor prognosis.[1]

The gelding was discharged with instructions to administer flunixin meglumine orally q24 for 4 days, TMS orally q12 until finished, and aspirin orally q24 for 5 days following resolution of catheter site swelling. His owners were to hot pack his catheter site for 10 minutes q12 following resolution of swelling and apply diclofenac sodium following each hot packing. His fecal and urine output were to be monitored daily along with his temperature. A primarily forage (fiber) and fat-based diet was recommended. Cereal grains and molasses-based feeds were to be avoided. Recommended pelleted feeds included: Nutrena SafeChoice, Purina Equine Senior, and Purina Strategy due to a higher crude fiber and fat content and low starch/sugar

content. A ration balancer like Amplify could be used to provide additional energy upon his return to performance level of work. Horses should receive a high-quality grass hay or mixed alfalfa-grass hay at 1-2% of their body weight daily. It was advised that the gelding have a gradual return to work over a 2.5-3 month time period. First with low intensity walks which he should maintain for a few weeks, and then the reintroduction of brief trots before reaching his full level of normal work. After his return to full level of work, he should be exercised at that same level of intensity daily, and he should not receive extended rest periods. Note that frequency should be increased in his exercise sessions before increasing the duration of them. After months of a slow return to normal work, following a strict exercise regime and diet the gelding has made a full recovery, without relapse.

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