One Leg to Stand On

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Case Description:

A 2-year-old Quarter Horse mare in training as a Western Performance horse was evaluated for acute onset of non-weight bearing lameness of the left thoracic limb during training. Evaluation of referring veterinarian diagnosed luxation of the left forelimb proximal interphalangeal joint and subsequently bandaged the limb and placed in a Kimze leg saver splint. Upon referral with a 2 hour trailer ride the patient presented with right front, right hind and left hind dropped fetlock joints.

Clinical Findings:

A 2-year-old Quarter Horse mare who presented to MSU-CVM Equine Emergency department on April 16, 2019 after referral for a luxation of her left thoracic proximal interphalangeal joint diagnosed radiographically (Figure 1) . The patient was lunging, and her trainer heard an audible pop and the mare was subsequently non-weight bearing in the left forelimb. The injury was characterized as an acute non-weight-bearing lameness (lameness score[1] 4/5) on her left thoracic limb. At time of referral the patient was bandaged and placed in a Kimzey Leg Saver®. There was no history of lameness prior to this isolated event. The patient was intended to be used as a Western Pleasure performance horse and was currently in ground training for the past 30 days. The mare was administered 1.1 mg/kg Flunixin Megulmine intravenously along with Butorphanol 0.01 mg/kg and Detomindine 0.01 mg/kg IV prior to transport.

During the initial physical examination, the horse was bright, alert, and painful, and all vital parameters were within reference limits. The patient's body condition score was 5/9. Her heart rate and respiratory rate were within normal limits with a pulse of 44 beats per minute, and

a respiration rate of 20 breaths per minute. Her temperature was not taken due to anxious demeanor. Her weight was approximated to be 800lbs but not taken due to extreme instability ambulating. No discharge was noted from her eyes or nose and she had pink mucous membranes with a capillary refill time of less than two seconds. Thoracic auscultation revealed a normal cardiac rhythm with normal bronchovesicular sounds. Abdominal auscultation was normal with borborygmi in all four quadrants.

Upon unloading from the trailer, three of the four extremities were dropped at the level of the metacarpophalangeal and metatarsophalangeal joints with the toe aspect of the hoof not in contact with the ground and she was unstable ambulating. Her lameness score was (lameness score[1] 4/5. The Kimzy splint was present on the left thoracic limb.

A baseline complete blood cell count (CBC) was taken. Her fibrinogen was mildly low and her segmented neutrophils were mildly high. A serum biochemistry profile was also obtained. She had mild hypokalemia and a mildly decreased blood osmolality. She had moderately high creatinine and creatinine kinase, alkaline phosphatase level and was hyperglycemic.

Treatment and Outcome:

A 14-gauge, 5.5-inch catheter[a] was aseptically placed in the left jugular vein, and administration of butorphanol (0.01 mg/kg),, detomidine (0.01 mg/kg),, and acepromazine (mg/kg) intravenously. Due to the severity of the lameness the remainder of the evaluation was conducted within a heavily bedded stall. Once sedated the mare laid down within in the stall and maintained lateral recumbency during the examination with sedation alone. Ultrasonographic examination of the distal extremities revealed multiple focal hypoechoic defects in echogenicity within all suspensory ligaments as well as the deep digital flexor tendons. Significant suspensory

ligament desmitis and disruption was noted in all four limbs with evidence of sesamoid fractures in all proximal sesamoids except for the left thoracic limb that presented in the Kimze Leg Saver. In effort to create stability for the mare. The left thoracic limb luxation of the proximal interphalangeal joint was reduced manually, then placed within a bandage cast incorporating the hoof to just below the head of the metacarpals. Additionally, the right thoracic limb was cast in a similar manor in order to stabilize the patient during diagnostic work up.

Left metatarsophalangeal joint radiographs (5 views) were obtained and interpreted as sesamoiditis to the lateral proximal sesamoid bones, proximal displacement of the proximal sesamoid bones from disruption to supporting ligamentous structures of the suspensory ligament, straight and oblique sesamoidean ligaments. There was intracapsular soft tissue swelling evident by the synovial effusion. There was also extracapsular soft tissue swelling. This was consistent with type 3 base fracture of the sesamoid bones. (Figure 2)

Due to the extreme extent of injuries sustained to all limbs the owners elected to humanely euthanize the mare.

Additional diagnostic testing in the form of genetic evaluation was collected at the time of euthanasia. Owing to the extreme joint laxity and severe degeneration of all suspensory ligaments the mare was suspect to be a HERDA affected horse. Hair samples were collected and submitted for genetic evaluation. The mare tested N/HRD carrier: horse carries one copy of the HERDA gene.

Necropsy Findings:

Necropsy revealed quadrilateral subcutaneous hemorrhage and edema of the metacarpophalangeal and metatarsophalangeal joints (Figure 3). There was quadrilateral hemorrhage and swelling of the suspensory ligaments. There were proximal sesamoid

fractures of the right thoracic and right pelvic and left pelvic limbs. Histologic lesions of the suspensory ligaments had multifocal interseptal and intercollagenous proteoglycan deposition with mineralization and osseous metaplasia of multifocal collagen bundles. Multifocal marked interstitial hemorrhage and edema with multifocal vascular degeneration, mineralization, vascular smooth muscle hypertrophy, and vascular proliferation was present. The deep digital flexor tendon and superficial digital tendon and tendon sheaths had multifocal vascular proliferation with marinating proteoglycan deposition and fibrosis. The aorta had multifocal tunica media degeneration and disorganization with multifocal suspect proteoglycan accumulation. The eye and nuchal ligament displayed no significant histologic lesions.

Histologic description:

Suspensory ligaments: Three separate suspensory ligaments were examined. All sections demonstrate similar histologic features. The suspensory ligaments of the left forelimb and both hindlimbs are multifocally expanded by zones of interstitial hemorrhage and edema. Intercollagenous septae are frequently prominent and consist of increased numbers of small caliber blood vessels. Small caliber vessels are frequently marginated by occasional small stellate to spindle cells (fibroblasts or tenoblasts) and increased amounts of pale basophilic to amphophilic acellular material (proteoglycan) and are present in close proximity to larger arterioles displaying markedly thickened smooth muscle walls. Occasional prominent arterioles also contain disrupted/fragmented elastin fibers. Occasional arterioles that are marginated by hemorrhage are transmurally mineralized. In all three suspensory ligaments examined, randomly scattered collagen bundles contain collagen that is interspersed with and multifocally replaced by pale

basophilic to amphophilic amorphous to acellular material (proteoglycan), scattered heavily stippled material (mineral), and occasional clusters of pale amphophilic chondrocytes. Individual chondrocytes have abundant amounts of clear to lightly basophilic cytoplasm and a prominent oval nucleus with uniform chromatin and one or more small nucleoli. Mineral aggregates and chondrocyte clusters often marginate partially mineralized vessels. In areas of hemorrhage, scattered collagen fibers are small, hypereosinophilic, and fragmented. The neighboring synovial membranes are prominent, highly vascularized, and lined by hypertrophied synoviocytes.

Deep digital and superficial digital flexor tendons: In cross sections from two deep digital flexor tendons and superficial digital flexor tendons the marginating tendon sheaths are composed of eosinophilic collagenous stroma interspersed with increased amounts of pale eosinophilic disorganized fibrillar collagen fibers and increased numbers of small blood vessels that are occasionally marginated by pale basophilic to amphophilic proteoglycan. Increased numbers of small septal blood vessels multifocally are appreciated within the tendon body.

Aorta: The tunica media is multifocally composed of disorganized smooth muscle cells that are occasionally interspersed with increased amounts of extracellular pale eosinophilic material and occasional hemorrhage.

Clinical Relevance

This is a rare presentation of a massive quadrilateral suspensory breakdown in a young HERDA carrier. This should be considered in any young Quarter Horse with unknown HERDA status with a subluxated joint or tendino-ligamentous breakdown. Radiographs and ultrasound

are helpful in confirming a tendino-ligamentous breakdown injury, but definitive diagnosis requires histological examination of affected tendons and ligaments along with genetic testing. Although a definitive diagnosis was not made until necropsy and genetic testing. Based on the diagnostics performed, pain level and grave prognosis euthanasia and necropsy were elected.

Discussion

Hereditary equine regional dermal asthenia (HERDA) and degenerative suspensory ligament disease (DSLD) have been well described in horses. Horses with DSLD are typically older at presentation, approximately 7-15 years of age and do not have detectable changes in flexor tenons[7]. While HERDA is well documented in the integument with hyperextensible skin. Horses with HERDA are known to have hyperextensible joints, with reports of the decreased tendino-ligamentous tensile strength[8]. Complete disruption of the suspensory ligament of this magnitude has not been reported.

Horses with DSLD have excessive amounts of proteoglycans under histological examination of the suspensory ligament, superficial and deep digital flexor tendons, patellar and nuchal ligaments, cardiovascular system and sclera. Changes in diameter of collagen fibrils, demonstrated in electron microscopy in tendons lead to increased permeability and proteoglycans. This is a systemic disorder that affects organs with connective tissue. The most prominent feature is an abnormal accumulation of proteoglycans between collagen and elastic fibers[3]. There has been an abnormal form of decorin identified in proteoglycan deposits[4]. This patient had multifocal interseptal and intercollagenous proteoglycan deposition within the suspensory ligaments, tendons shealths, superficial and deep digital tendons. This patient's nuchal ligament and sclera were normal, but the aorta displayed disorganization of the tunica media with areas of suspect extracellular accumulation of proteoglycan.

HERDA is a missense mutation in peptidyl-prolyl cis-trans isomerase B (PPIB), which encodes cyclophilin B and alters folding and post translational modifications of fibrillar collagen[5]. Clinical signs typically occur around 18 months of age as training begins while pressure is applied with a saddle. The most common site affected is the dorsum where ulcerations occur. Despite this horse not showing lesion to the integument, lower tensile strength in the tendino-ligamentous tissue is the suspected cause of this quadrilateral suspensory apparatus acute breakdown. Due to line breeding in cutting Quarter Horses, there is a higher concentration of carrier status within this population[6]. This horse was not HERDA tested prior and did not show any dorsum lesions.

Horses with HERDA have a significantly lower tensile strength in tendino-ligamentous tissues and lower elastic modules in great vessels[5]. Based off the history of her aorta and with lower elastic modules in great vessels, this mare would have been at risk for an aortic tear during her athletic career continued based off the histology of her aorta. In a study at MSU-CVM, the tensile strength of tendino-ligamentous structures was significantly reduced in horses with HERDA relative to control horses, which was consistent across the SDFT, DDFT and SL[6]. This is consistent with this case because the SDFT, DDFT and SL were all affected on this patient. HERDA is an autosomal recessive trait, meaning if two carriers (N/HRD) are bred, there is a 25% chance that the foal will be affected (HRD/HRD). When carriers are bred to normal horses 50% of their foals are expected to be carriers[2]. This mare's genetic testing came back as a carrier of one copy of the HERDA gene (N/HRD). Being a HERDA carrier may also explain her initial subluxation that untimely led to the remaining three legs to have flexor break down. At this time it is suspected that being a HERDA carrier led this patient to its massive tendino-ligamentous breakdown.

In conclusion, HERDA carrier or positive should be considered a differential diagnosis of massive tendino-ligamentous injuries in young horses. As evidence by the horse of this report, a basic radiographic evaluation of the metacarpus or metatarsus which consists of minimum number of projects are sufficient for sesamoid fractures. The importance of ultrasound to evaluate the integrity of the tendons is stressed. Ultimately, definitive diagnosis is made postmortem at the histological level and with genetic testing. Thus, it is recommended for any Quarter Horse of showing and breeding potential to submit a 5-panel equine genetic test. This includes; PSSM, HERDA, GBED, HYPP and MH.

Abbreviations

DSDL Degenerative Suspensory Ligament Desmitits
HERDA Hereditary Equine Regional Dermal Asthenia
MSU-CVM Mississippi State University College of Veterinary Medicine
SDFT Superficial digital flexor tendon
DDFT Deep digital flexor tendon
SL Suspensory Ligament
PSSM Polysaccharide storage myopathy
GBED Glycogen branching enzyme deficiency
HYPP Hyperkalemic periodic paralysis
MH Malignant hyperthermia

Footnotes

a. Xylazine, Akorn, Inc., Decatur, Illinois, USA
b. Acepromazine maleate, Henry Schein Animal Health, Dublin, Ohio, USA
c. Butorphanol, Fort Dodge Animal Health, a division of Wyeth, Pfizer Inc, New York, New York, USA
d. Flunixin meglumine, Intervet Inc., Merck & Co. Inc. Whitehouse Station, New Jersey, USA

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